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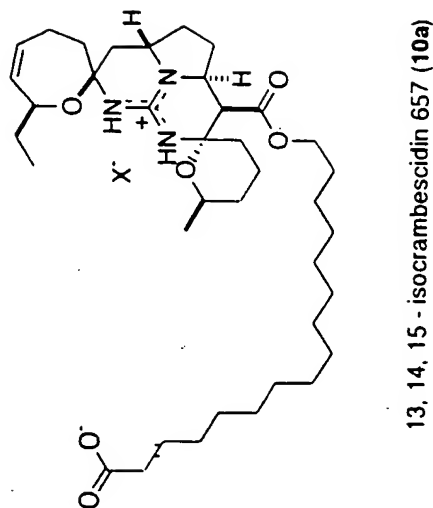
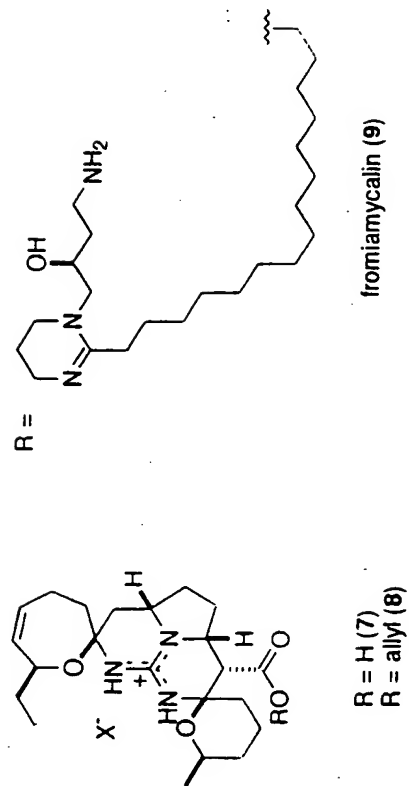
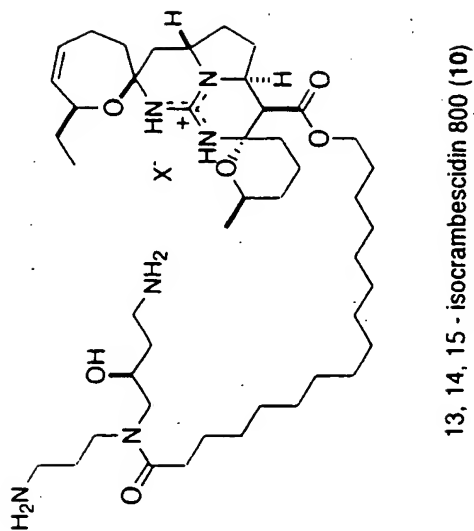
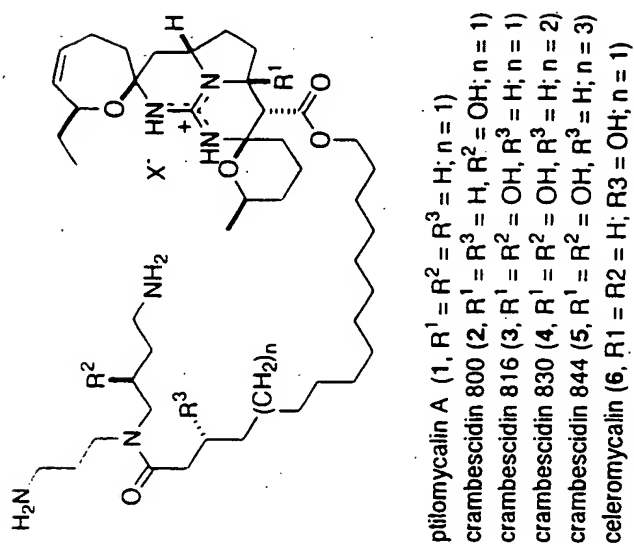


Figure 1

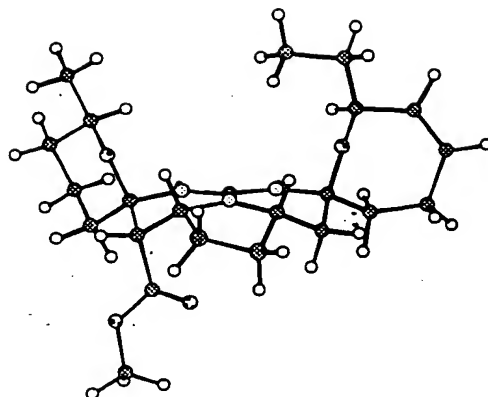


Figure 2

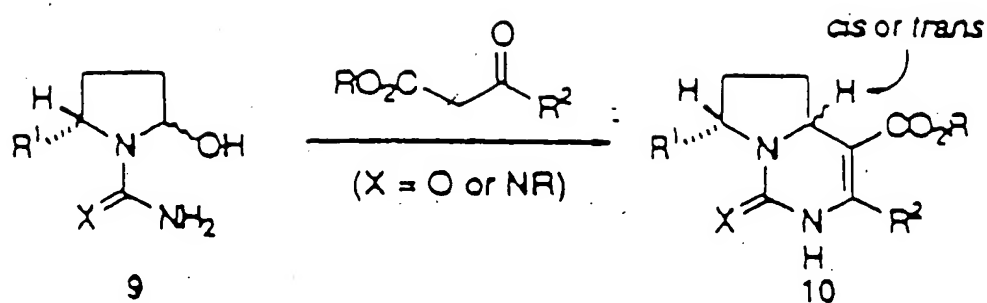
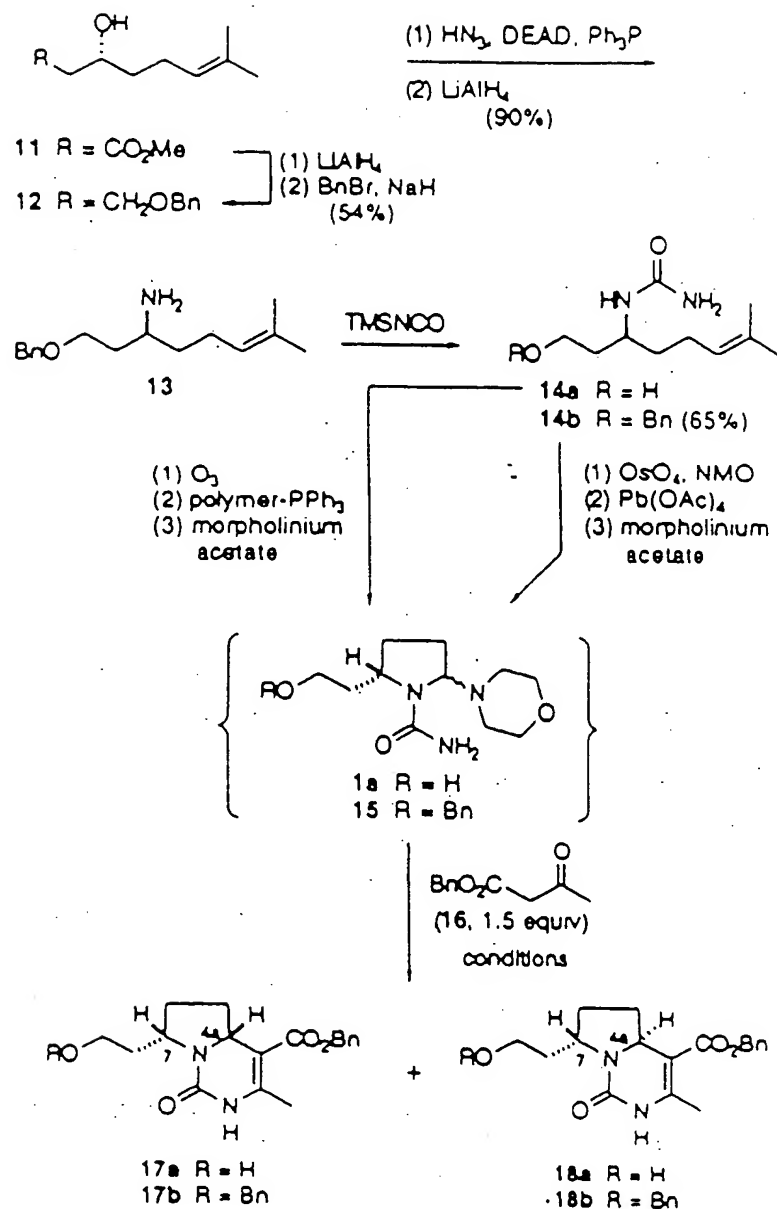


FIGURE .3



substrate	reaction conditions	17:18 (yield) ^a
1a	morpholinium acetate (1.5 eq),	4:1 (80%)
15	$\text{CF}_3\text{CH}_2\text{OH}$, 60 °C, 48 h	4:1 (81%)
15	PPE, CH_2CH_2 , 23 °C, 48 h	1:4 (60%)

^a Combined overall yield of 17 and 18 from 14.

FIGURE 4

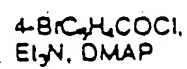
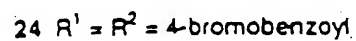
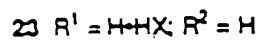
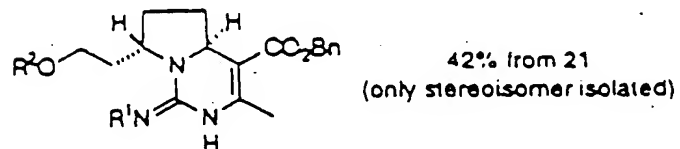
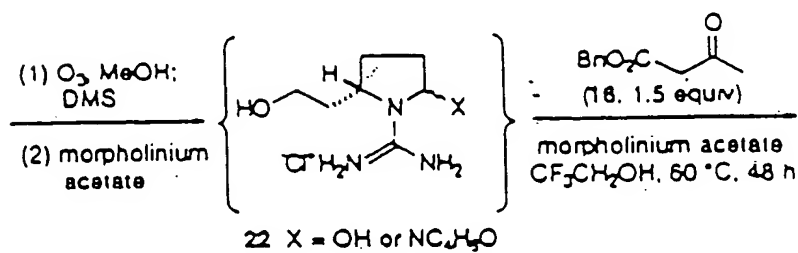
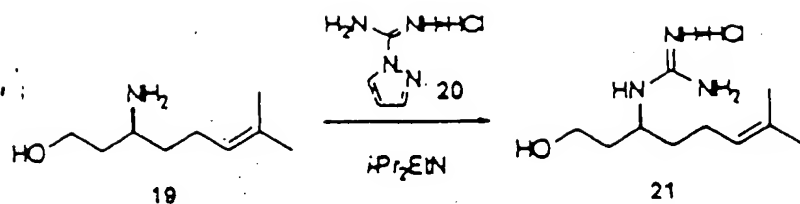
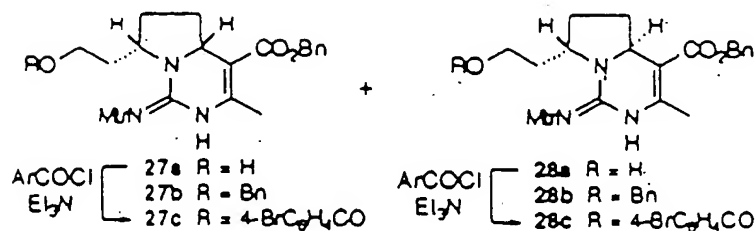
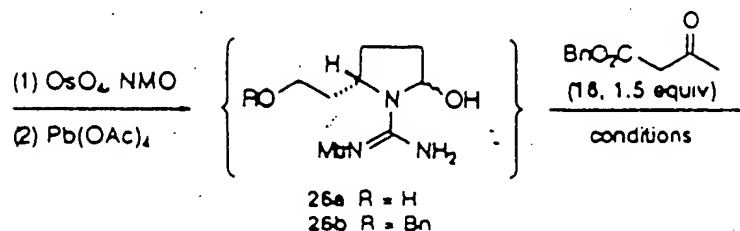
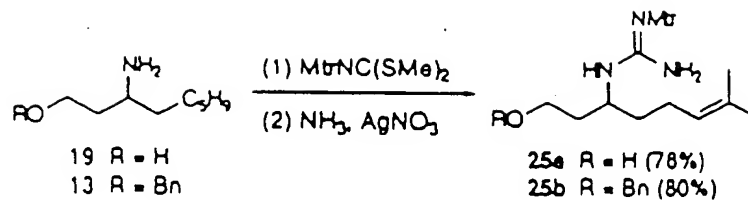


FIGURE 5



substrate	reaction conditions	27:28 (yield) ^a
26a	morpholinium acetate (1.5 eq),	6:1 (61%)
26b	CF ₃ CH ₂ OH, 60 °C, 48 h	7:1 (84%)
26b	PPE, CH ₂ Cl ₂ , 23 °C, 48 h	1:20 (61%)

^a Combined overall yield of 27 and 28 from 25.

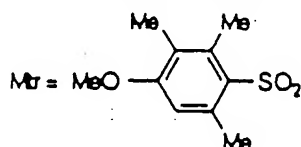


FIGURE 6

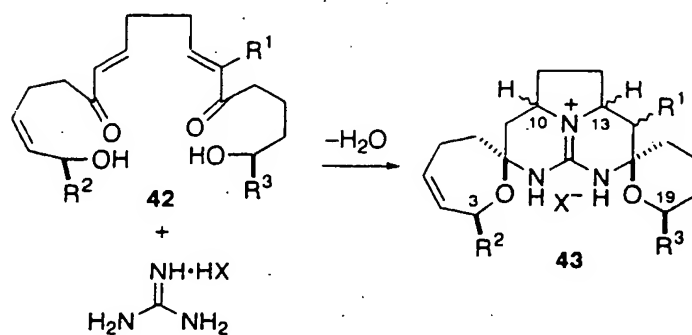
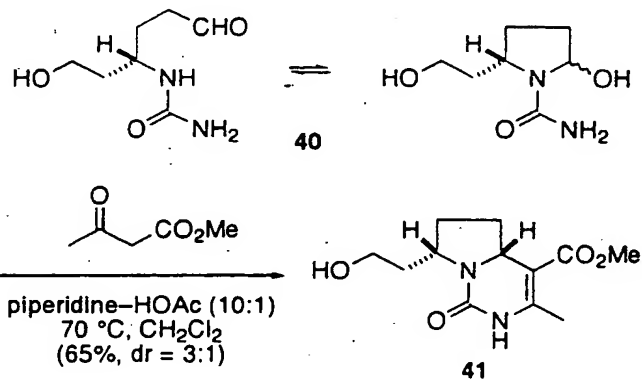
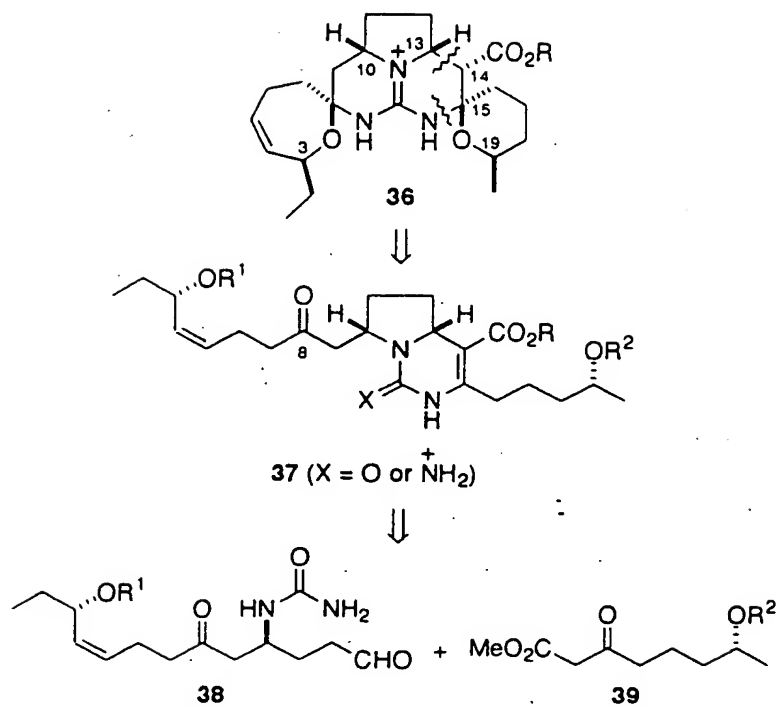


Figure 8

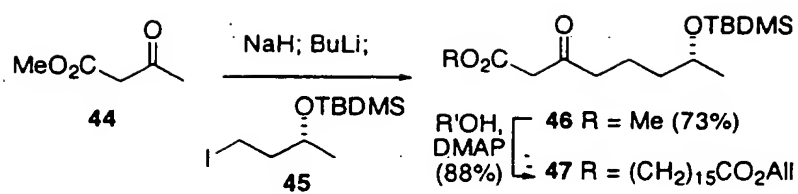


Figure 9



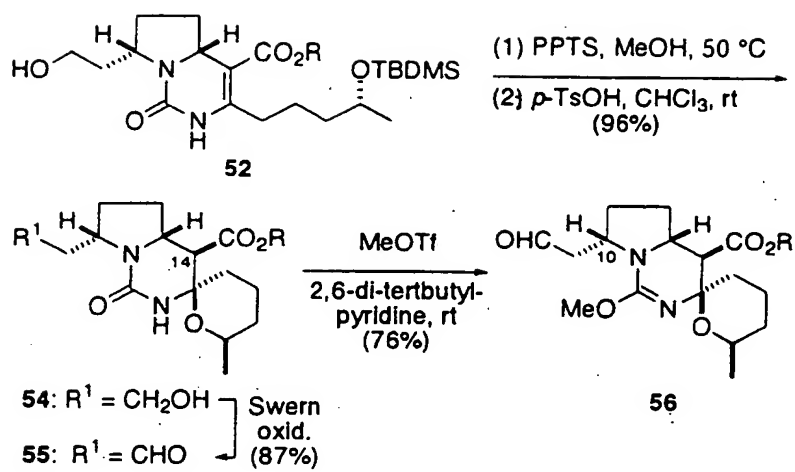


Figure 11

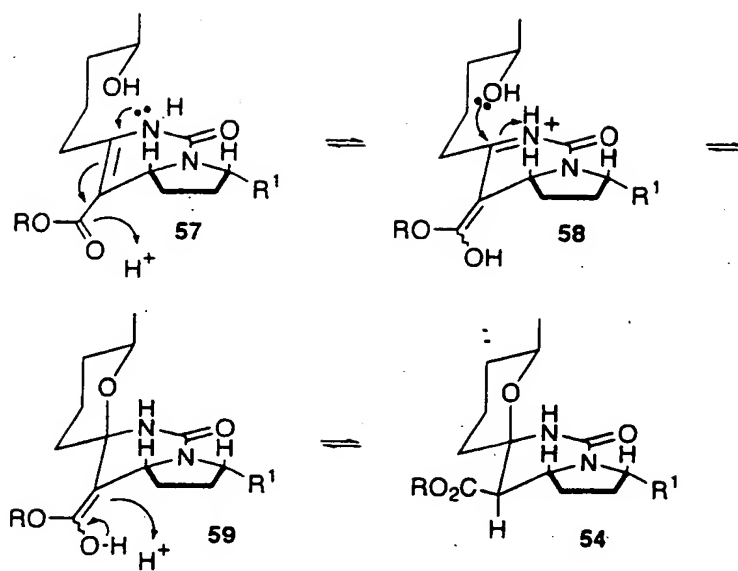


Figure 12

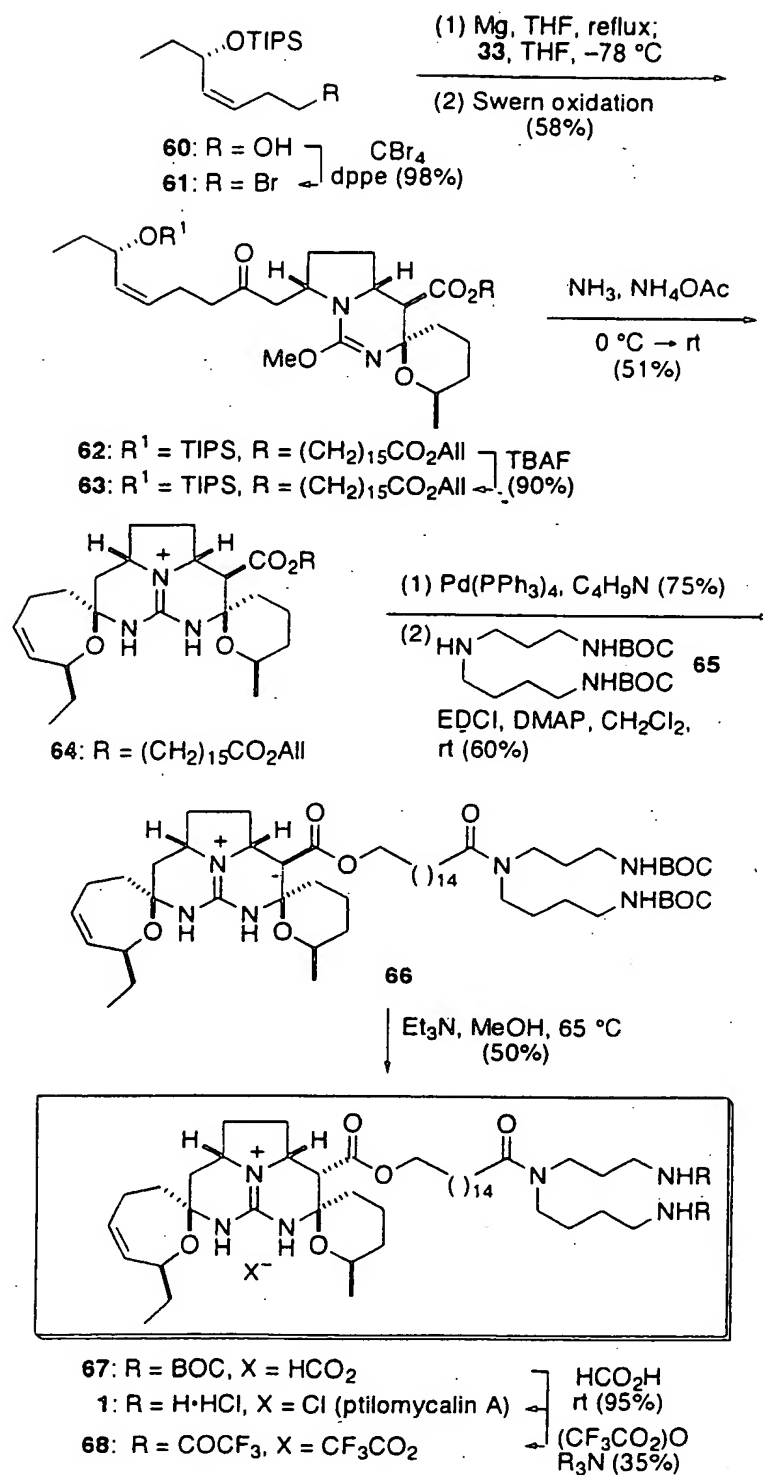


Figure 13

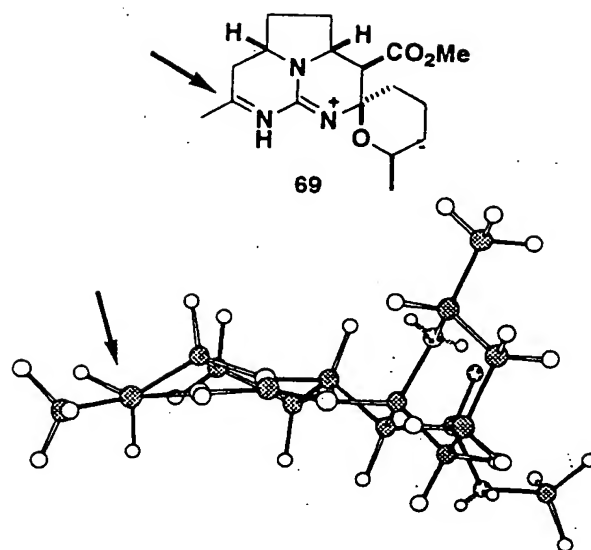


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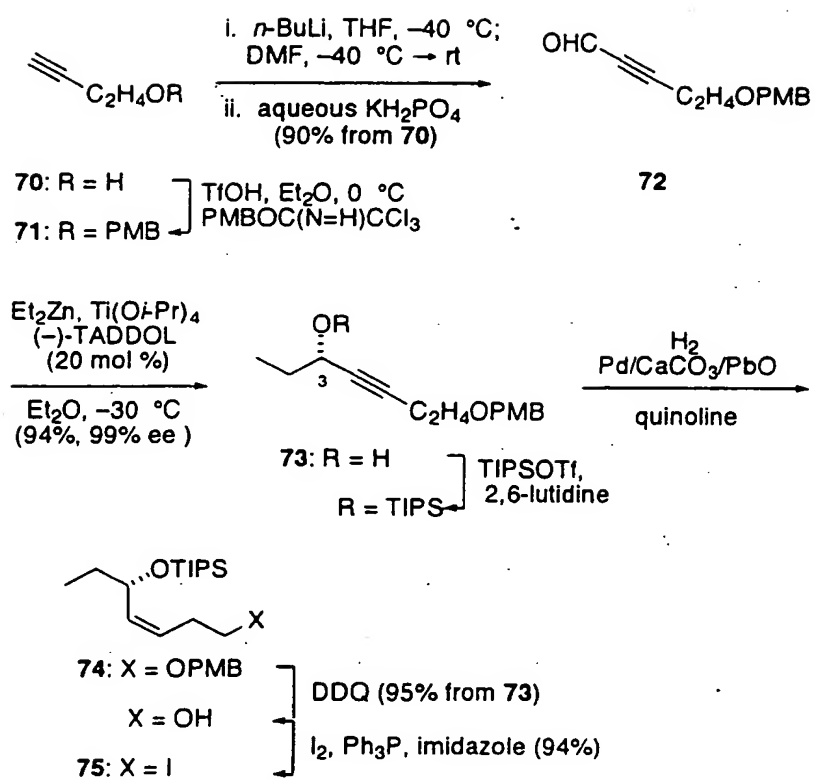


Figure 15

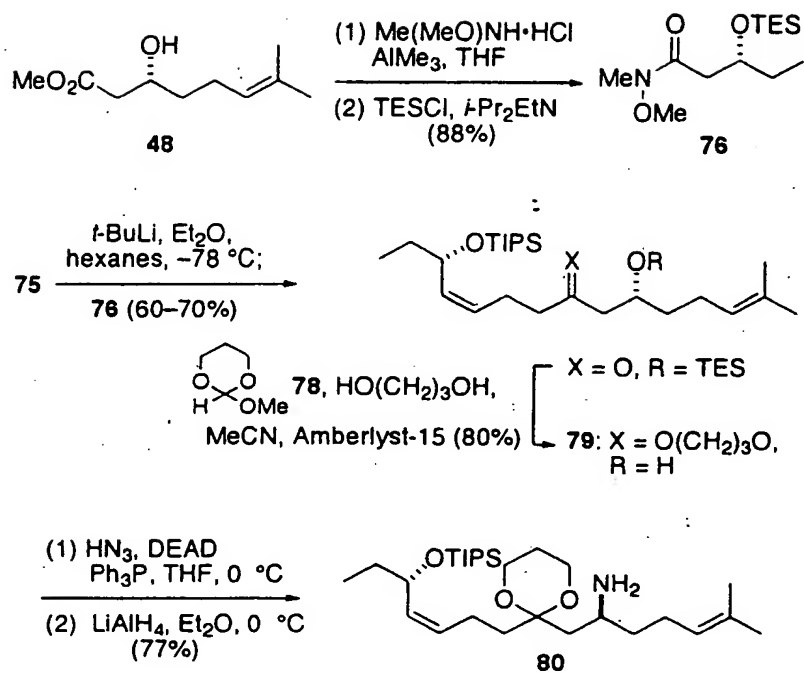


Figure 16

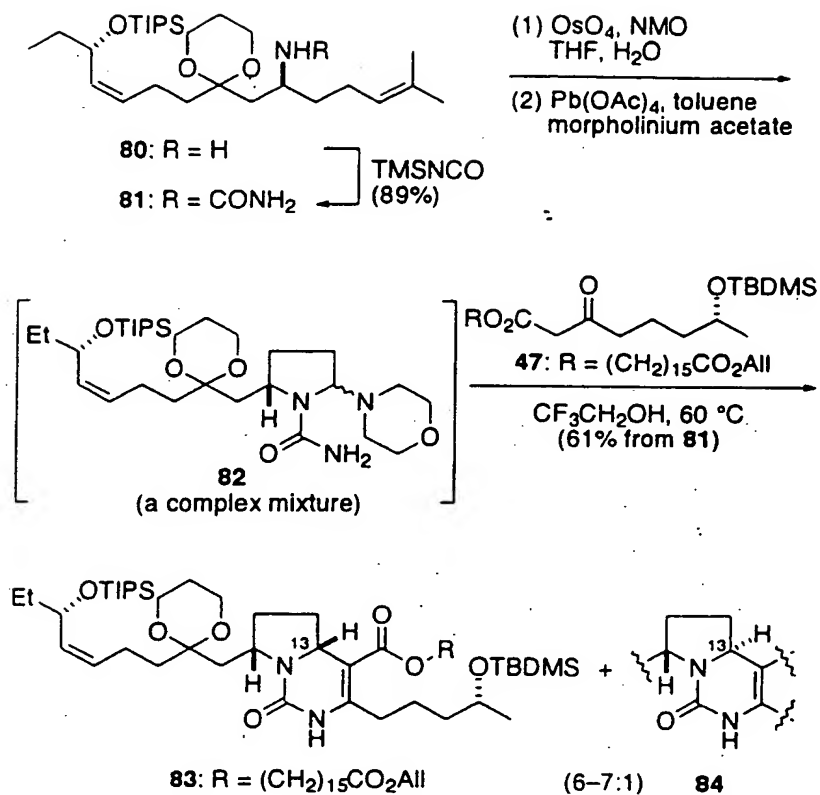


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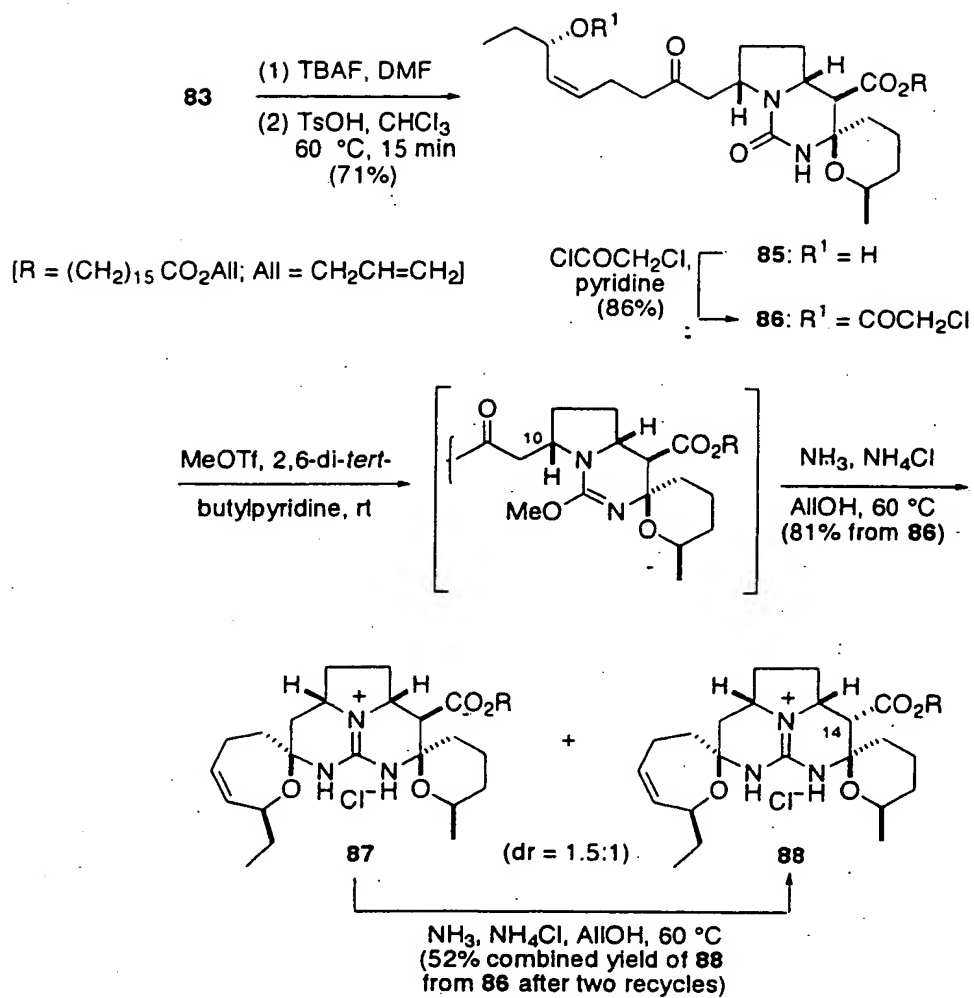


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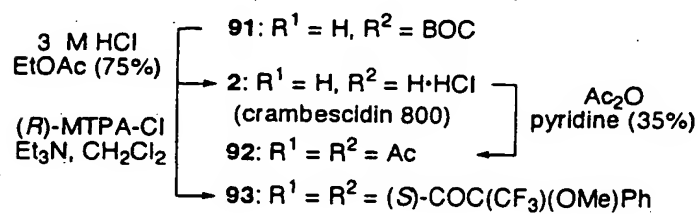
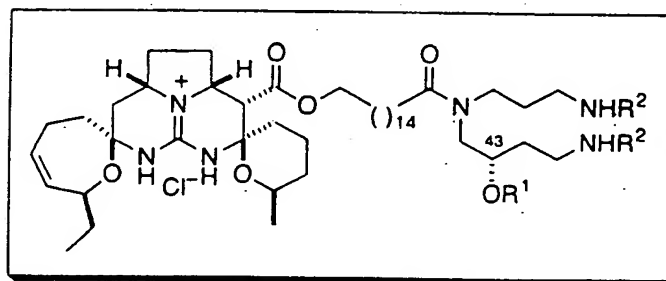
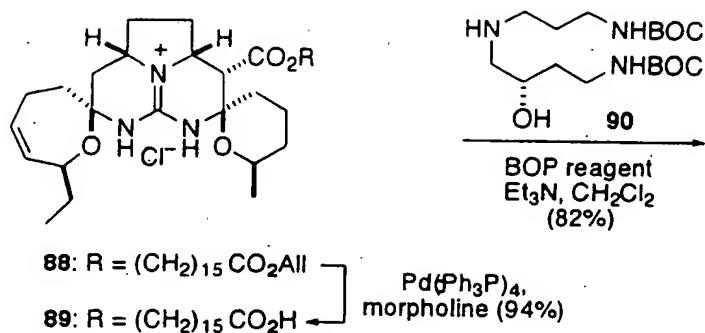
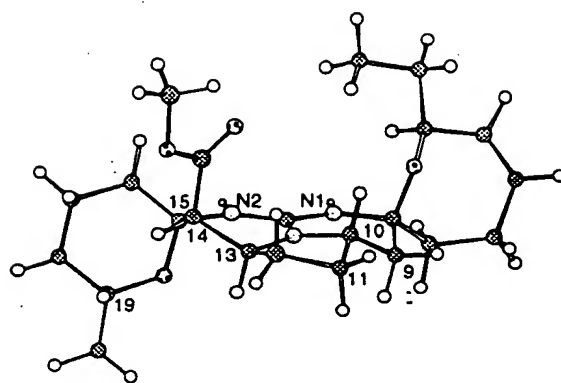
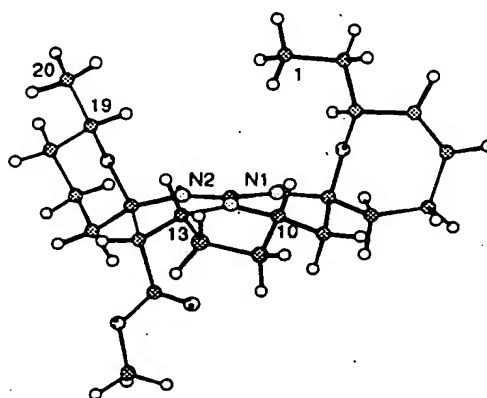


Figure 19



13,14,15-isocrambescidin core



crambescidin/ptilomycalin A core

Figure 20

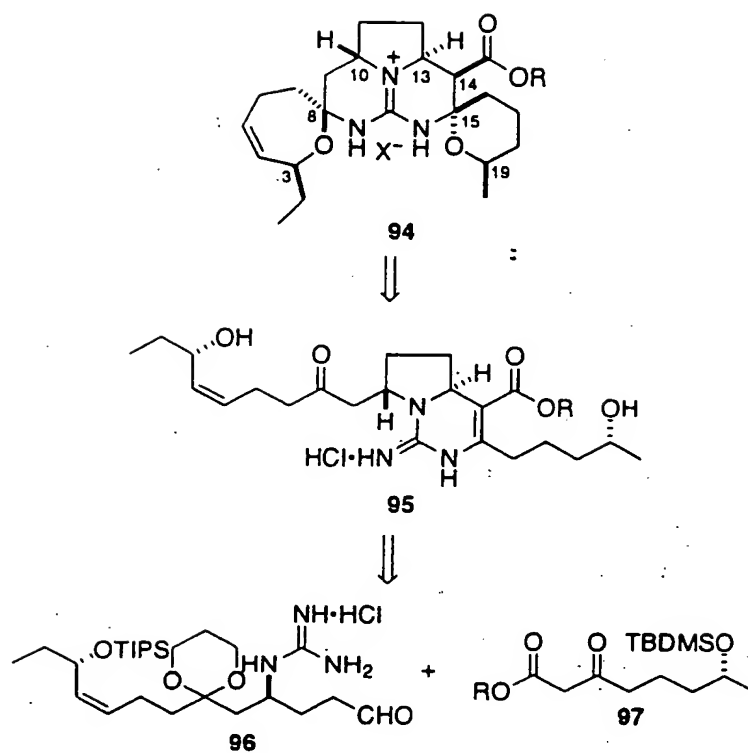


Figure 21

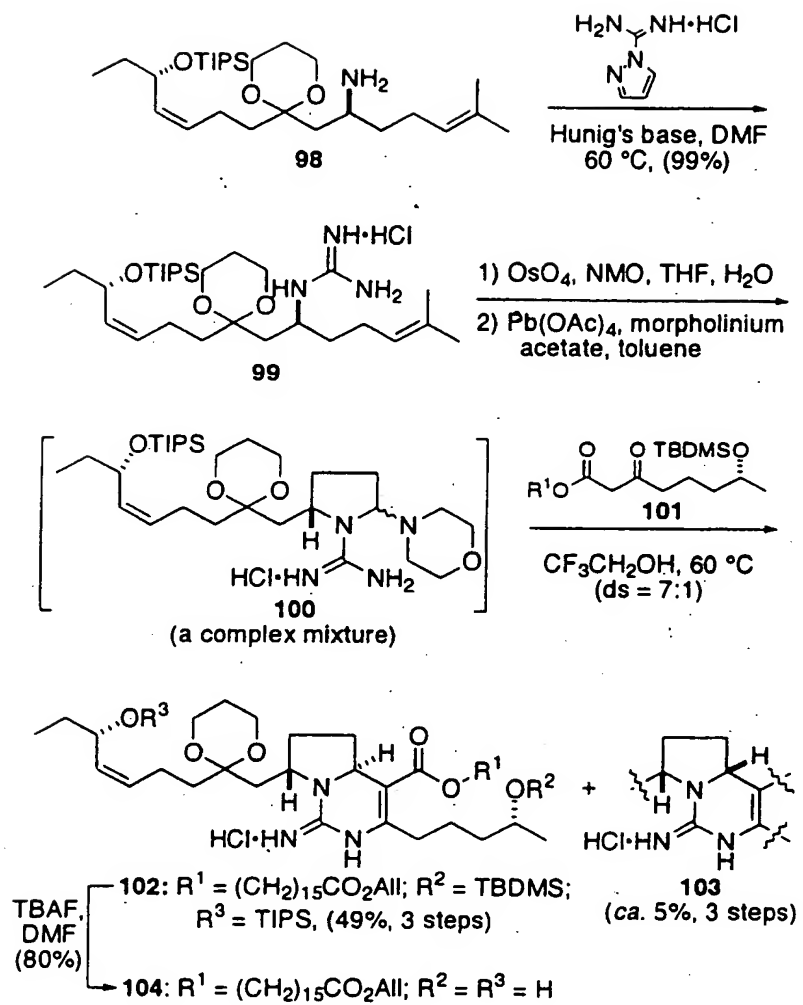


Figure 22

$R = (CH_2)_{15}CO_2AlI$

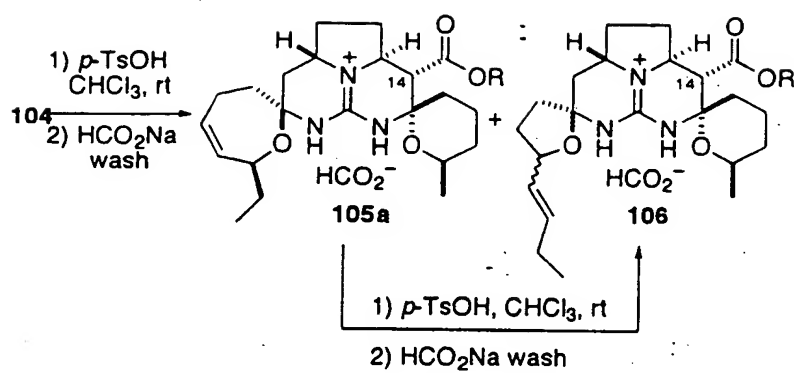


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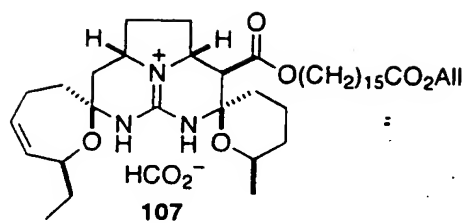
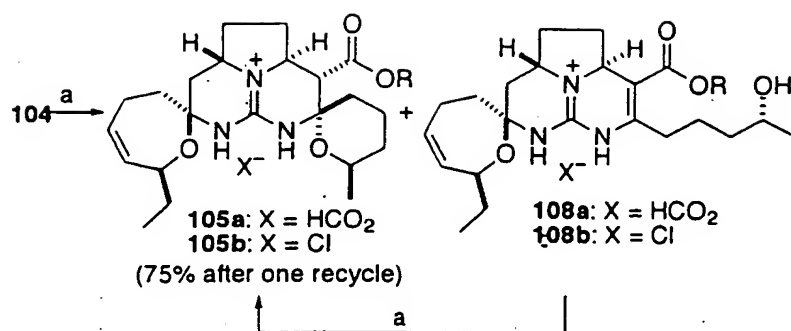


Figure 24

R = (CH₂)₁₅CO₂AlI



^aReagents: (a) PPTS, CHCl₃, 90 °C, 24 h; HCO₂ Na wash
or 0.1 N HCl wash

Figure 25

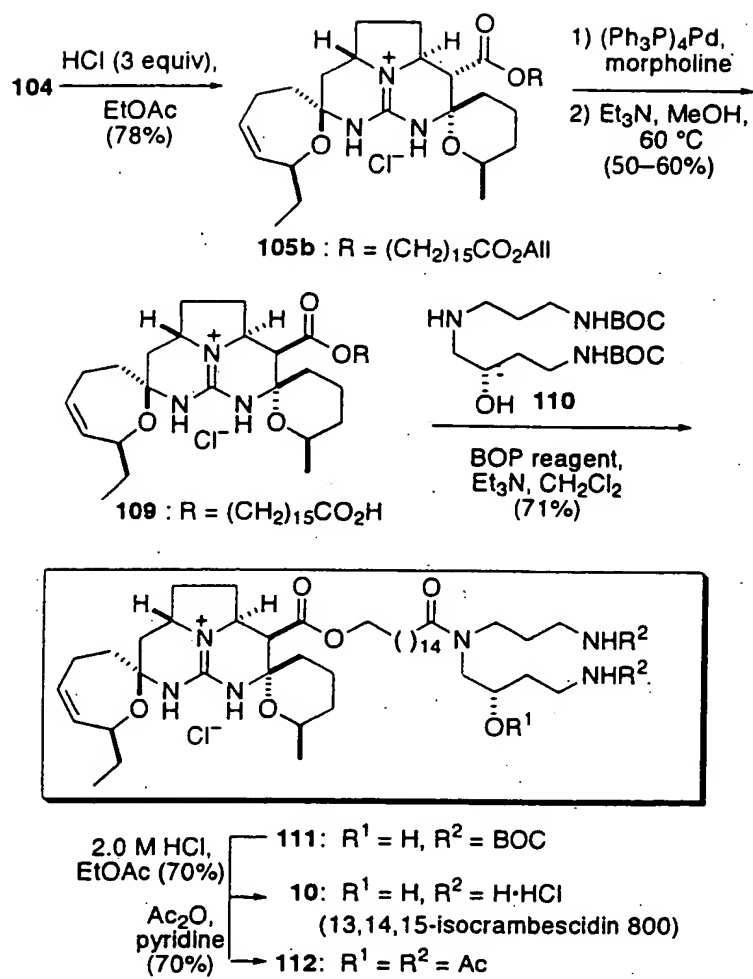


Figure 26

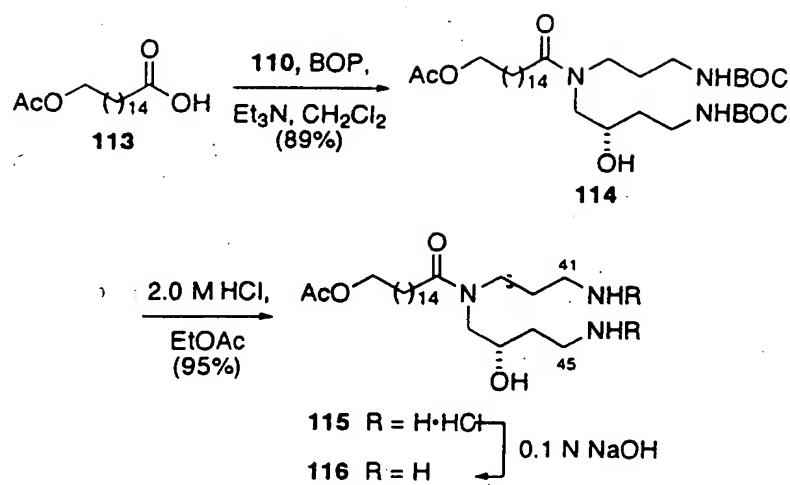


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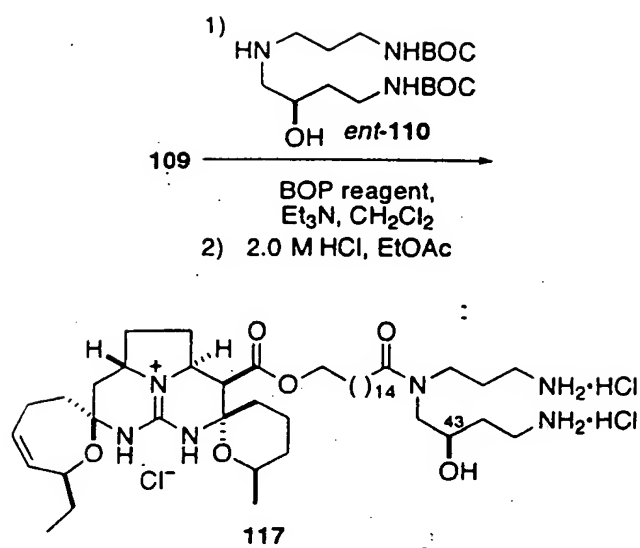
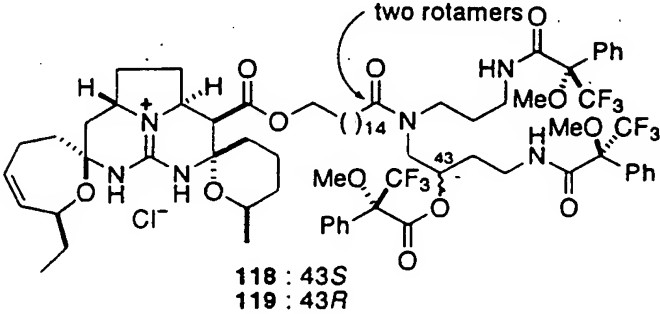


Figure 28

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		 <div> <div>118 : 43S</div> <div>119 : 43R</div> </div>	
entry	starting material	product	¹⁹ F NMR (CDCl ₃) ^a , δ ppm
1	synthetic 10	118	-68.77, -68.82 (2 peaks), -68.9, -70.5, -70.9
2	117	119	-68.6, -68.7, -68.8, -68.9, -71.0, -71.1
3	natural 10	118	-68.77, -68.82 (2 peaks), -68.9, -70.5, -70.9

^aDue to rotamers about the C38 amide, there are six peaks in the ¹⁹F NMR spectra.

Figure 29

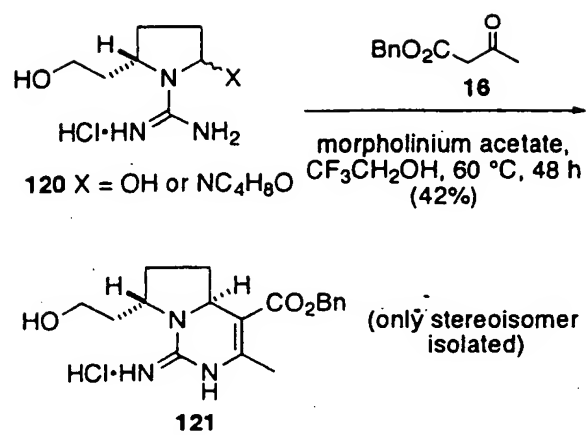
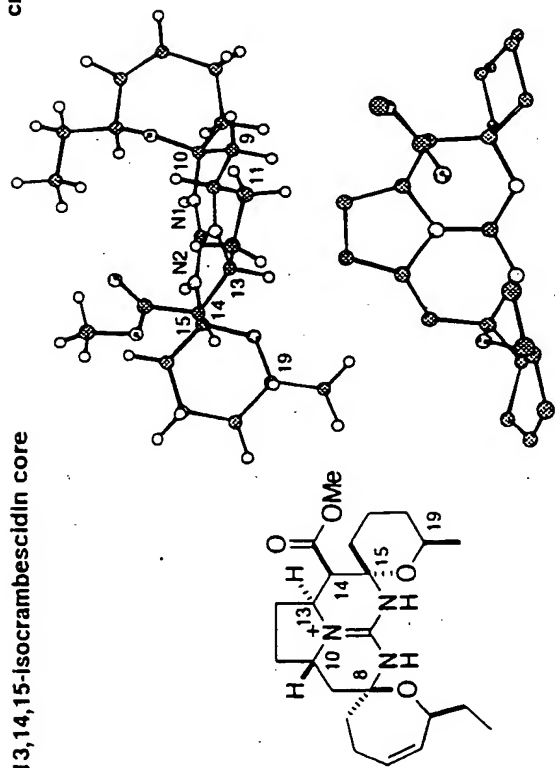
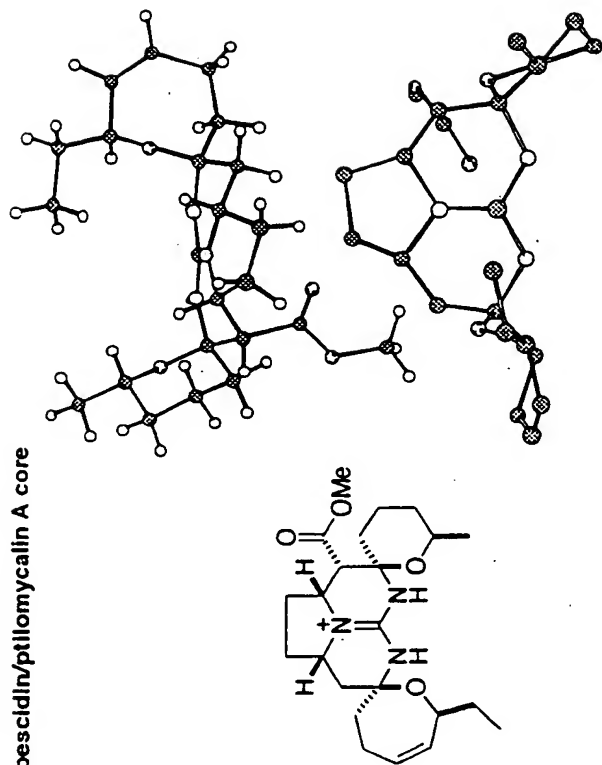


Figure 30

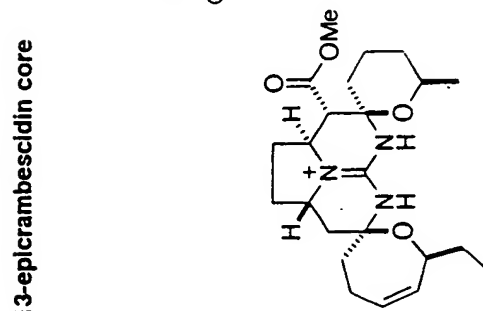
13,14,15-isocrambescidin core



crambescidin/ptilomycalin A core



13-epicrambescidin core



13,15-epicrambescidin core

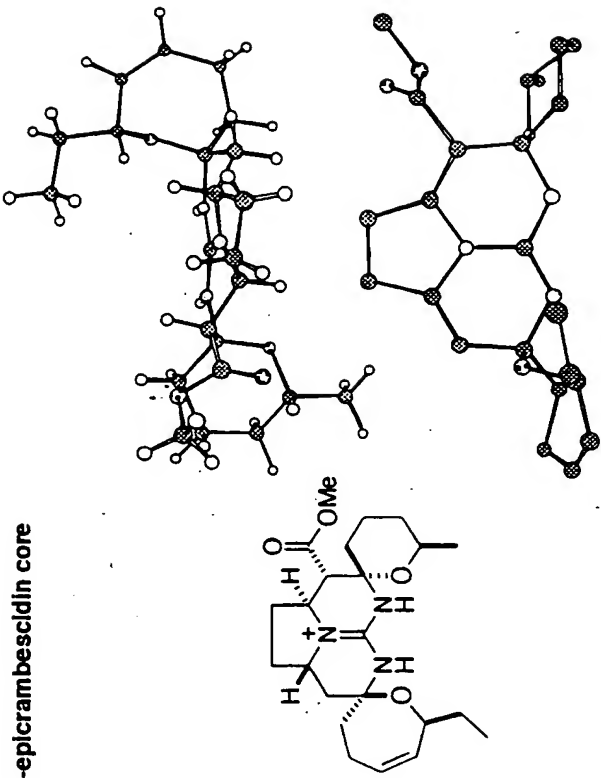


Figure 31

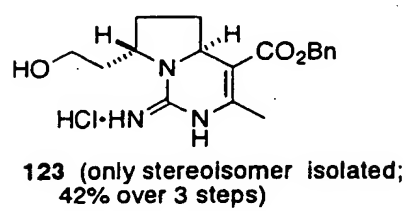
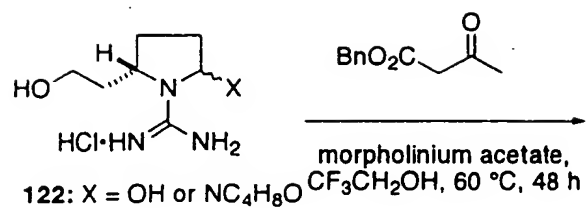


Figure 32

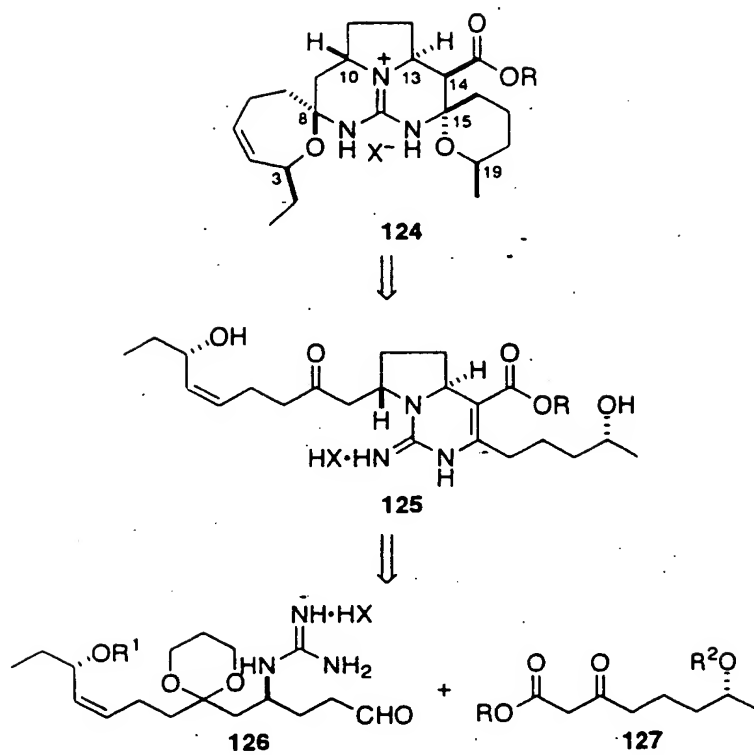


Figure 33

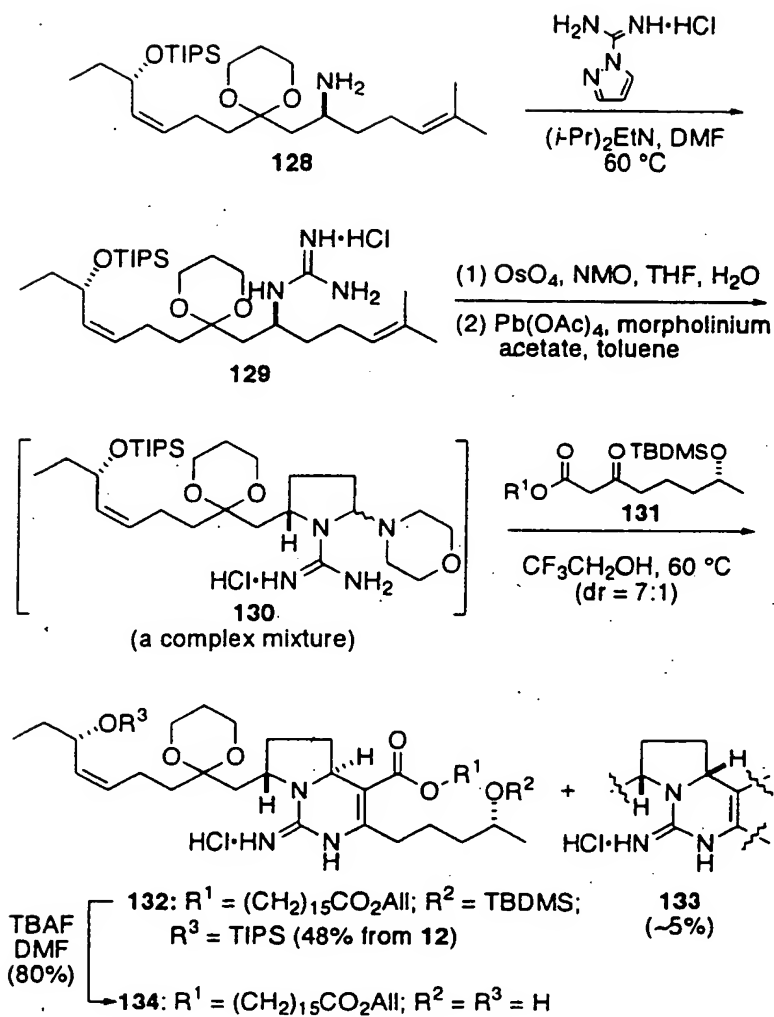


Figure 34

$R = (CH_2)_{15}CO_2All$

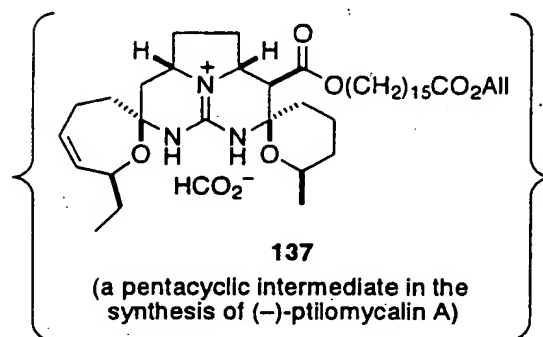
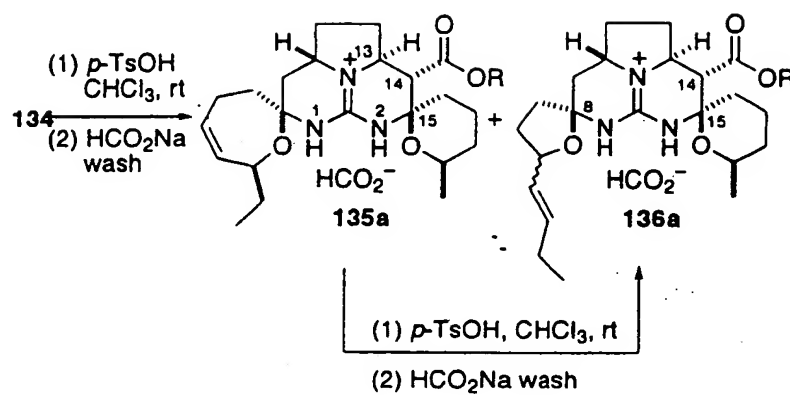
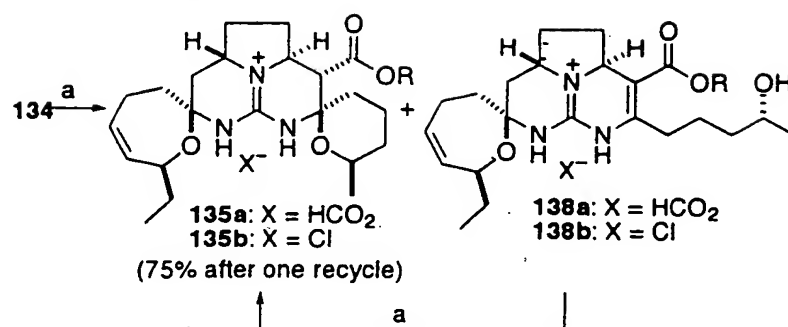


Figure 35

R = (CH₂)₁₅CO₂AlI



^aReagents: (a) PPTS, CHCl₃, 90 °C, 24 h; HCO₂Na wash or 0.1 N HCl wash

Figure 36

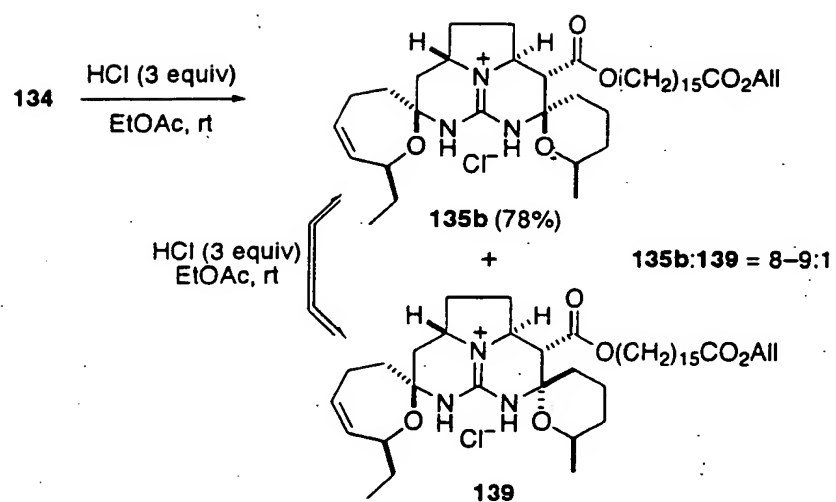
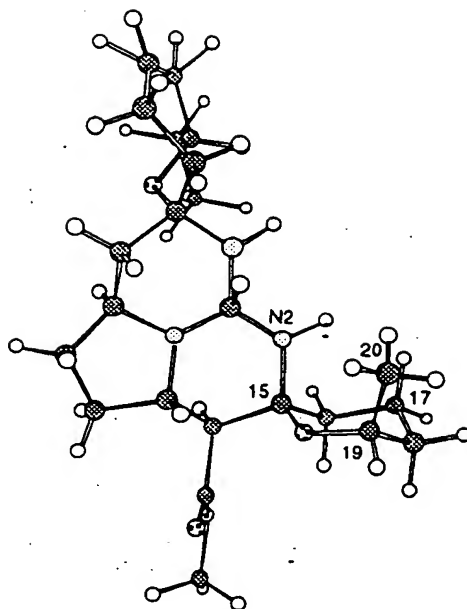


Figure 37

A



B

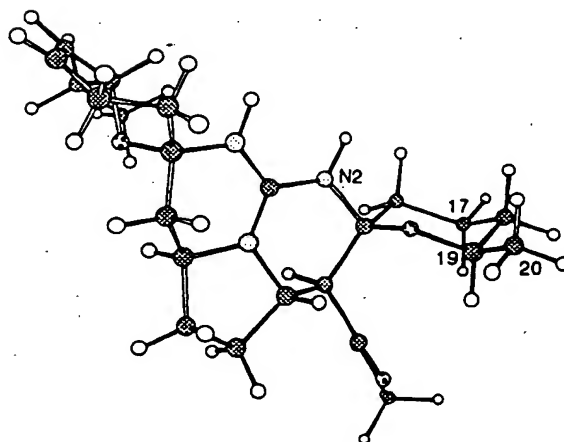
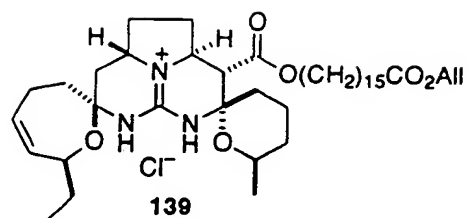
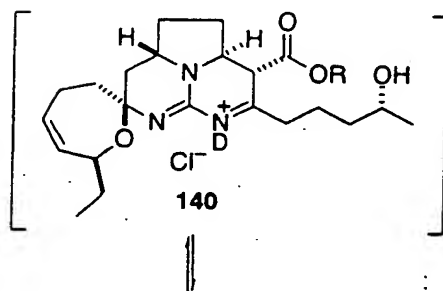


Figure 38



DCI, EtOAc
rt, 24 h



no deuterium
incorporation
at C14

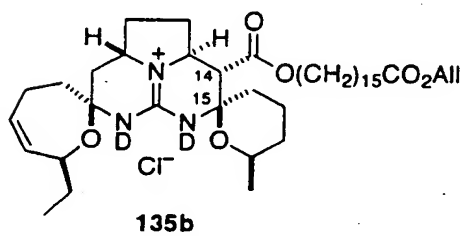


Figure 39

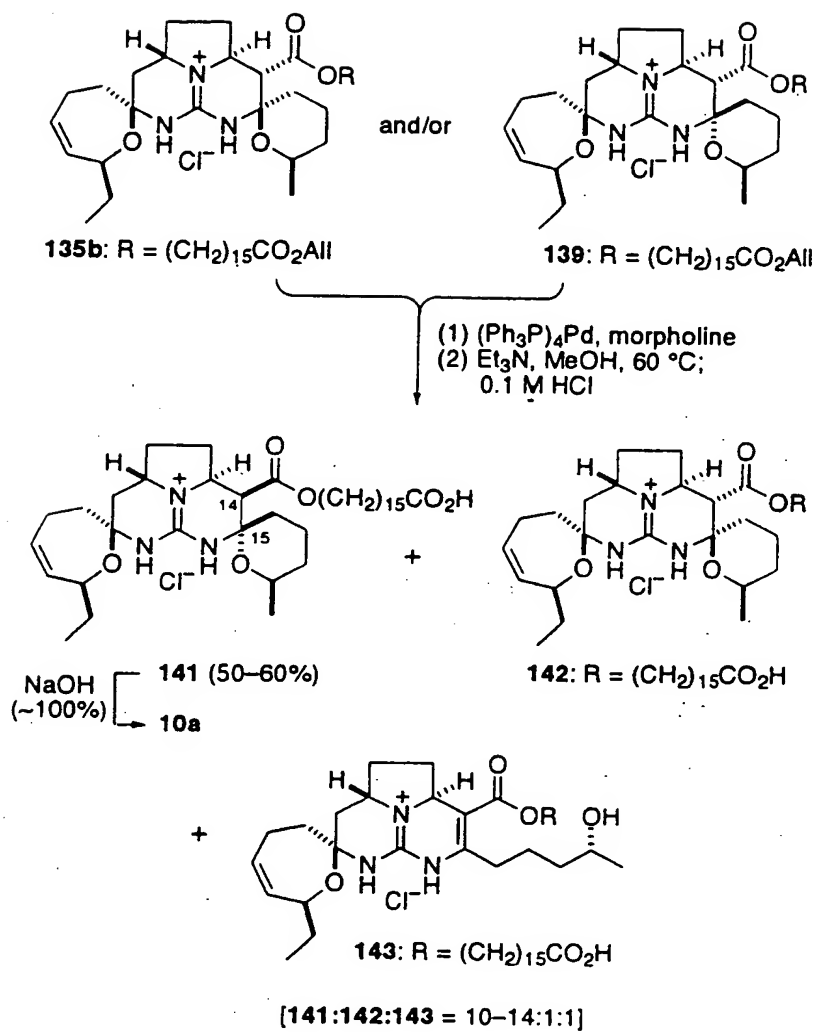


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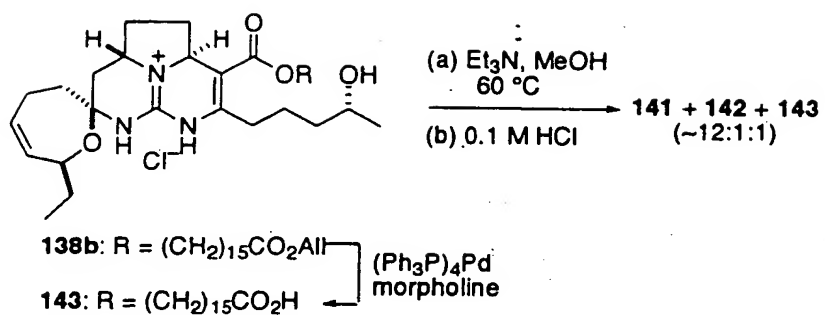


Figure 41

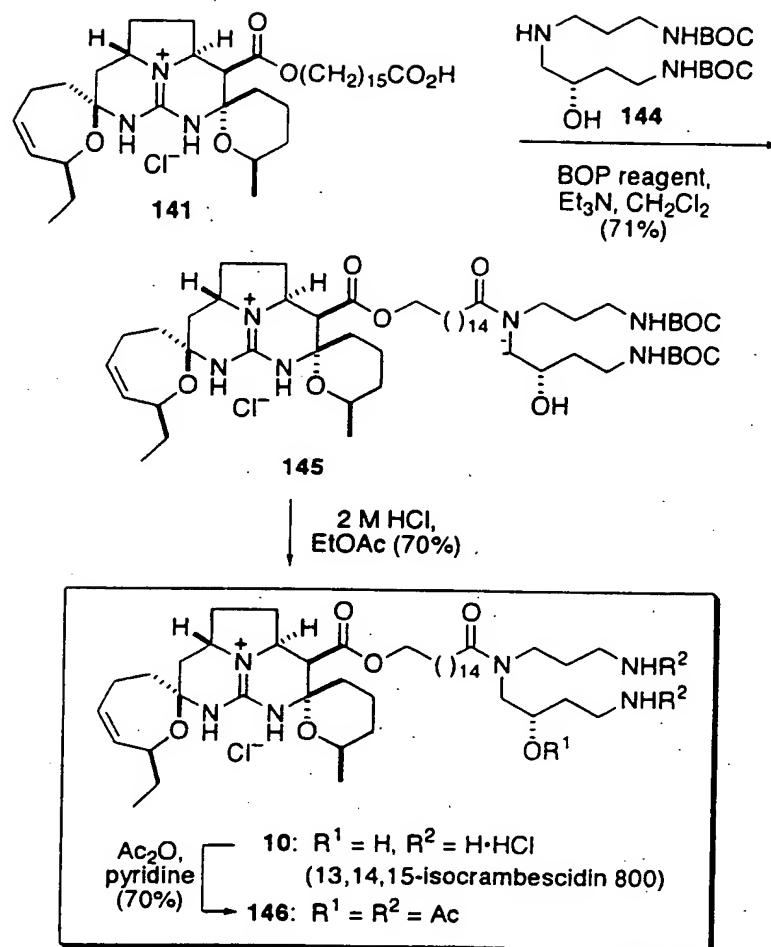


Figure 42

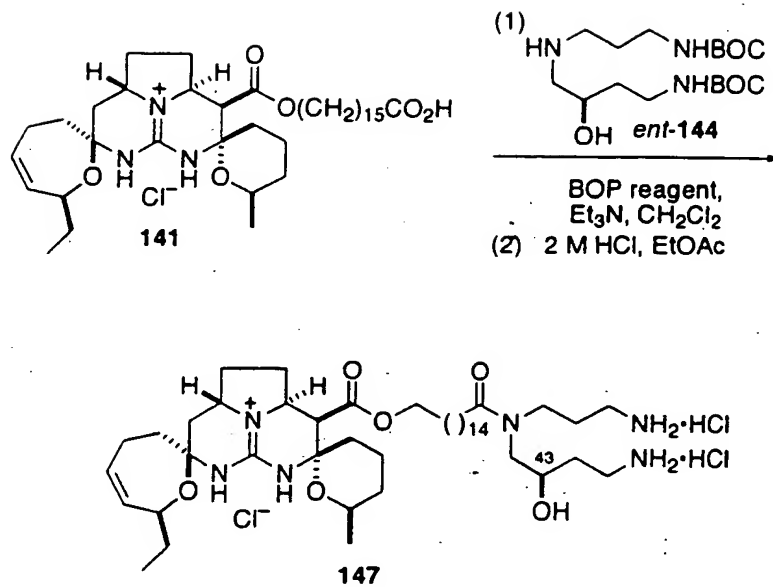
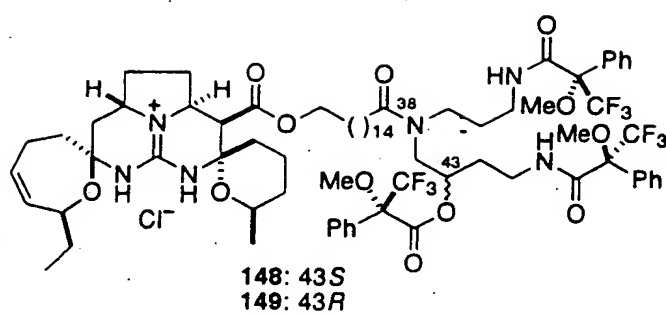


Figure 43



entry	starting material	product	^{19}F NMR (CDCl_3) ^a , δ ppm
1	synthetic 10	148	-68.77, -68.82 (2 peaks), -68.9, -70.5, -70.9
2	147	149	-68.6, -68.7, -68.8, -68.9, -71.0, -71.1
3	natural 10	148	-68.77, -68.82 (2 peaks), -68.9, -70.5, -70.9

^aDue to rotamers about the C38 amide bond on the NMR time scale, six peaks are observed in the ^{19}F NMR spectra.

Figure 44

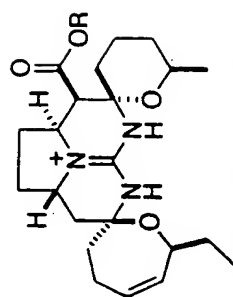
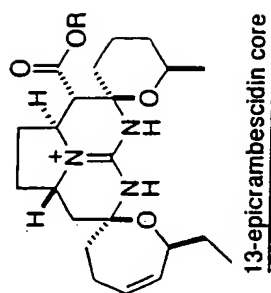
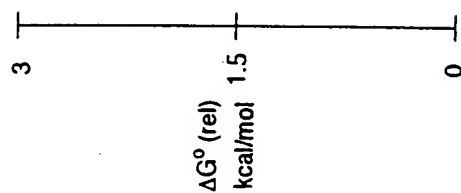
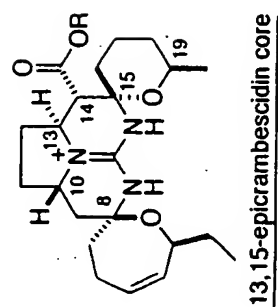


Figure 45

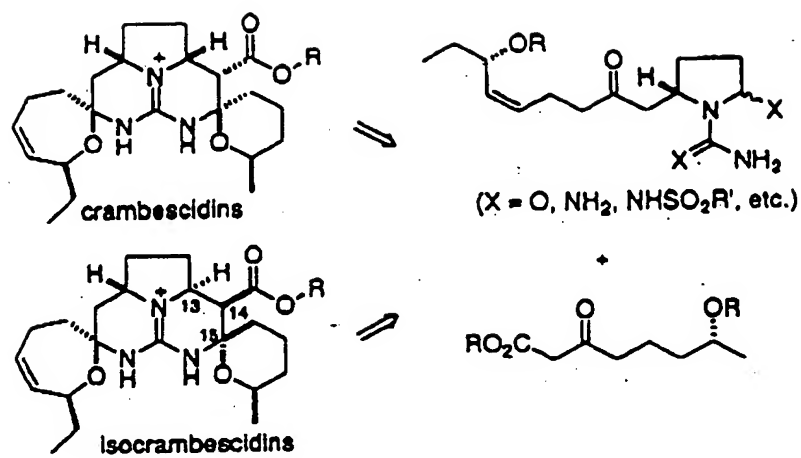


Figure 46



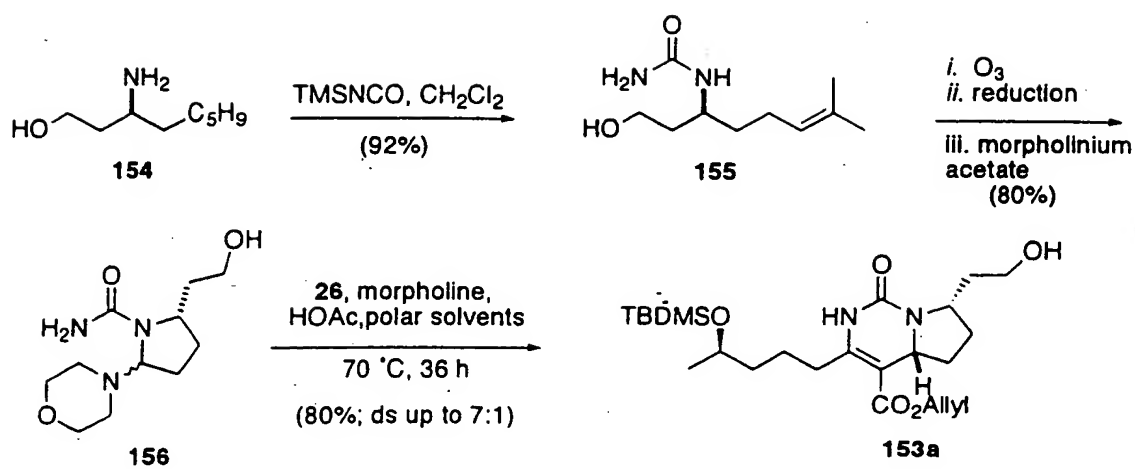


Figure 48

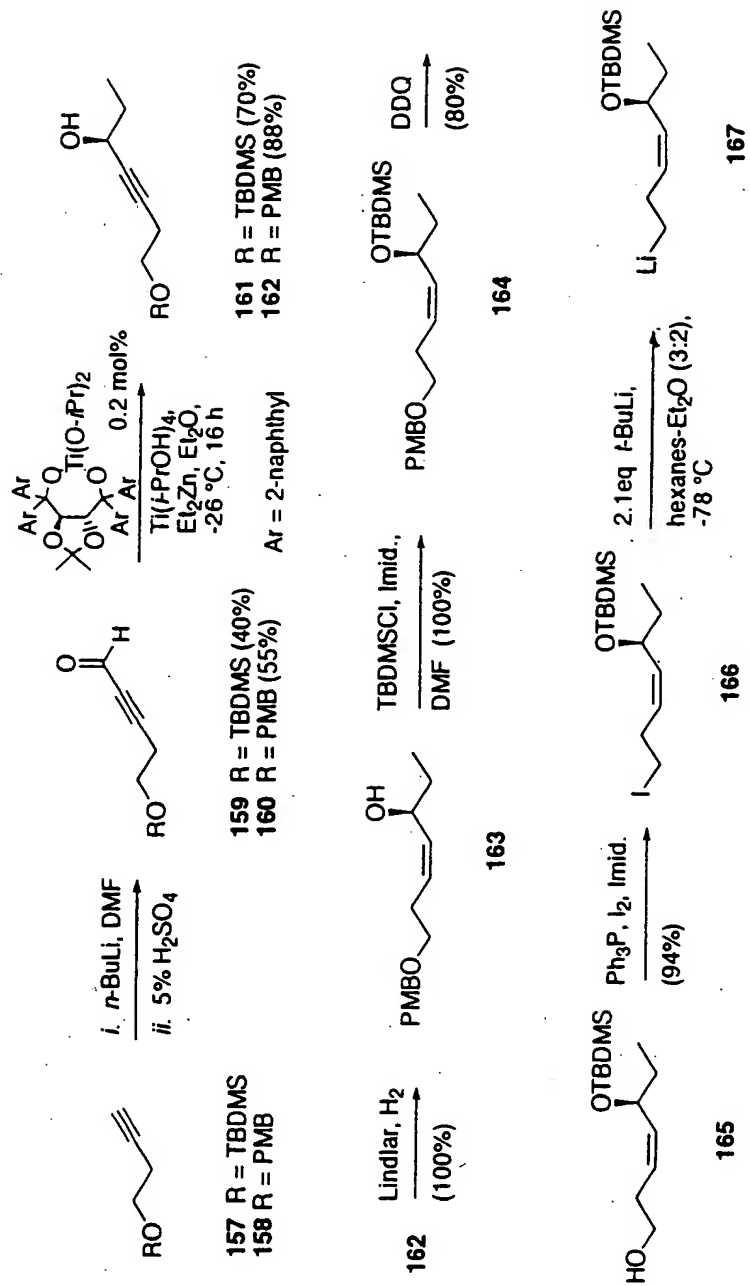


Figure 49

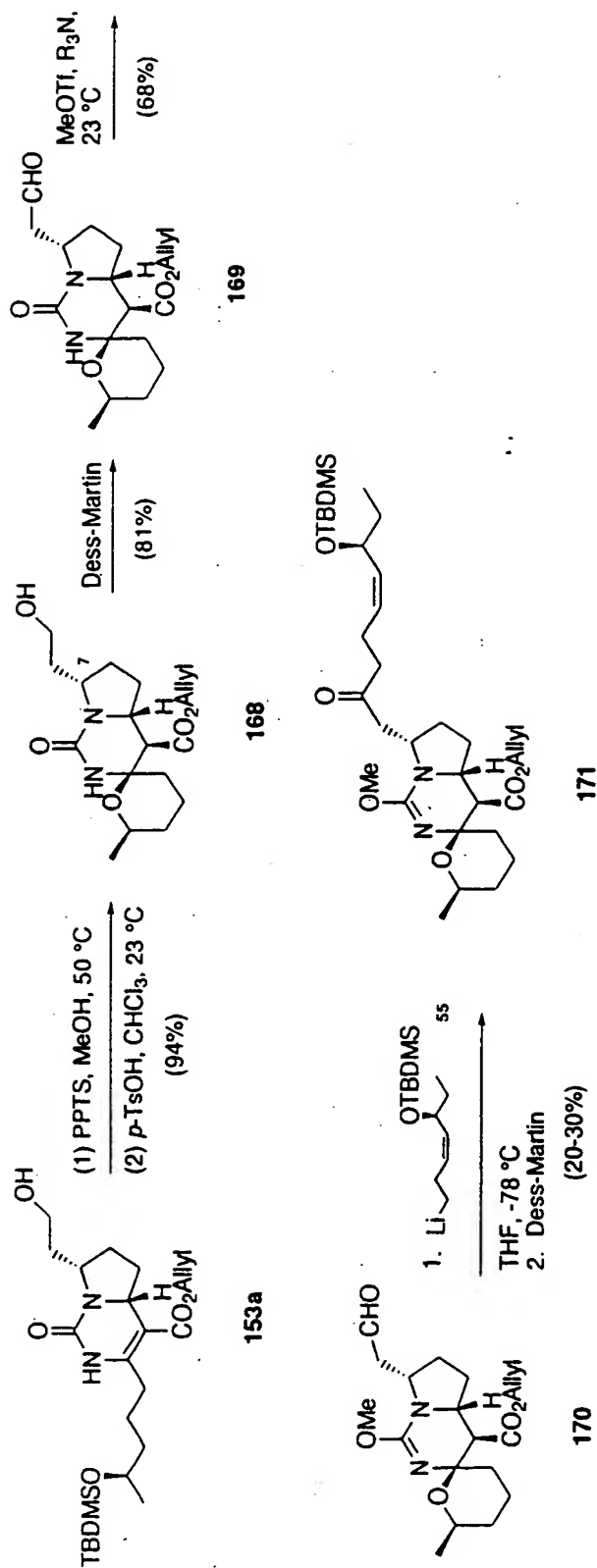


Figure 50

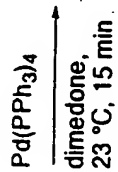
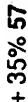


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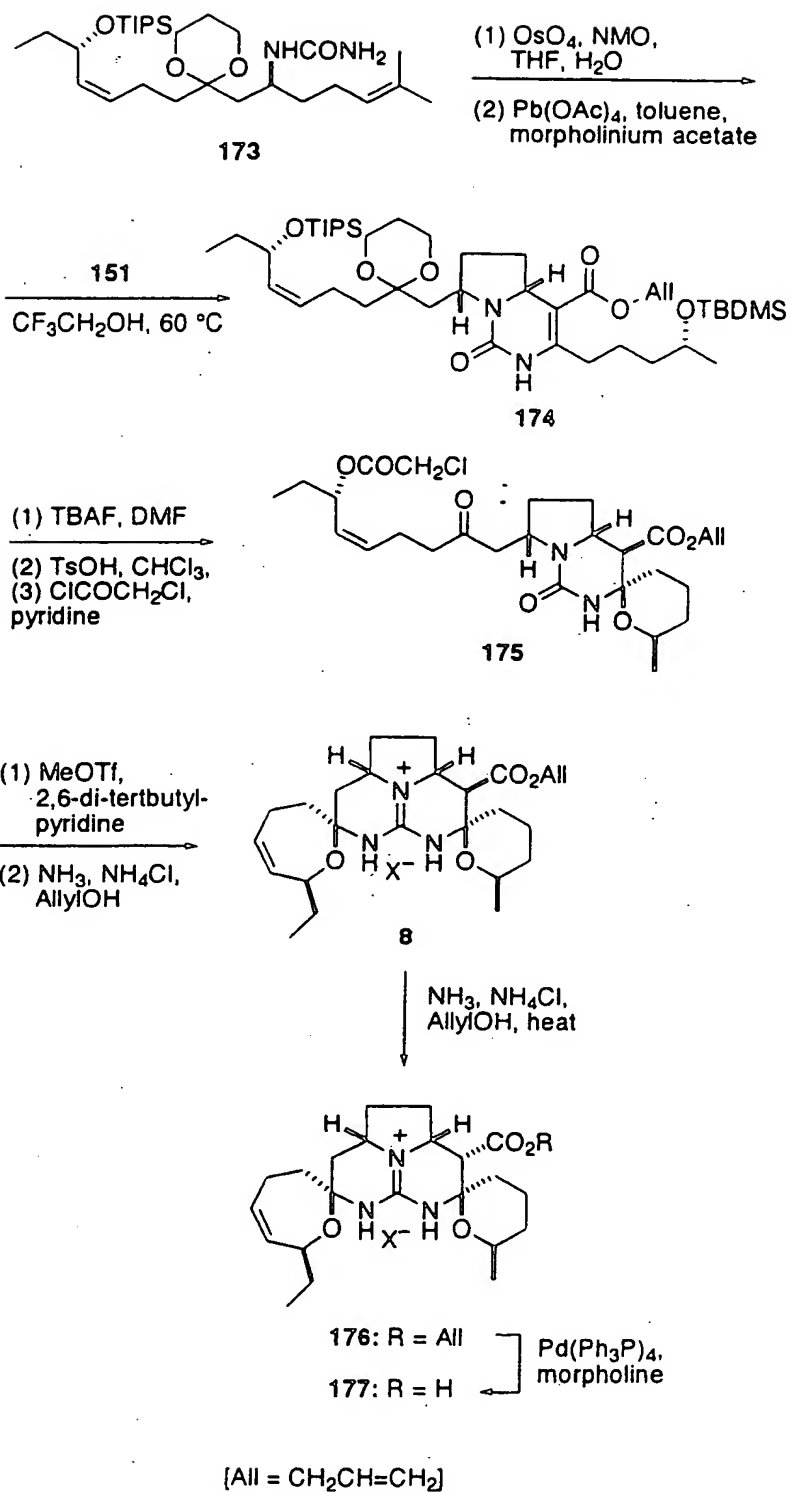


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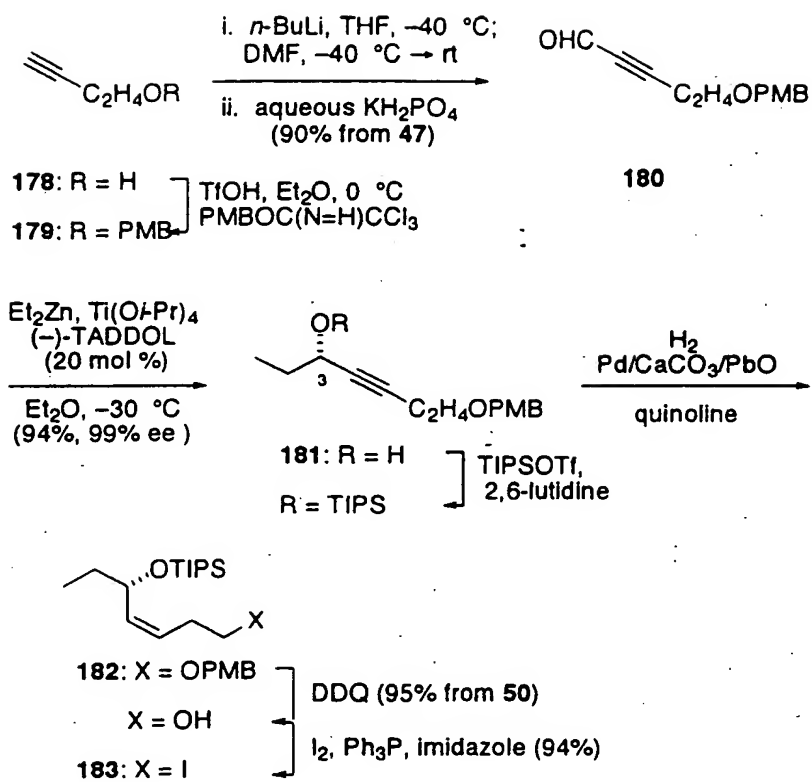


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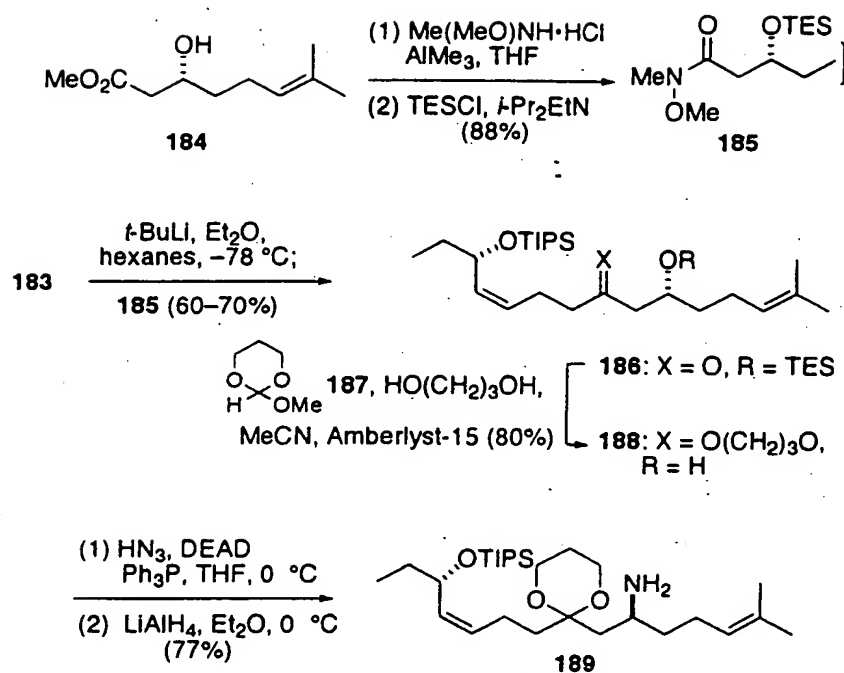


Figure 54

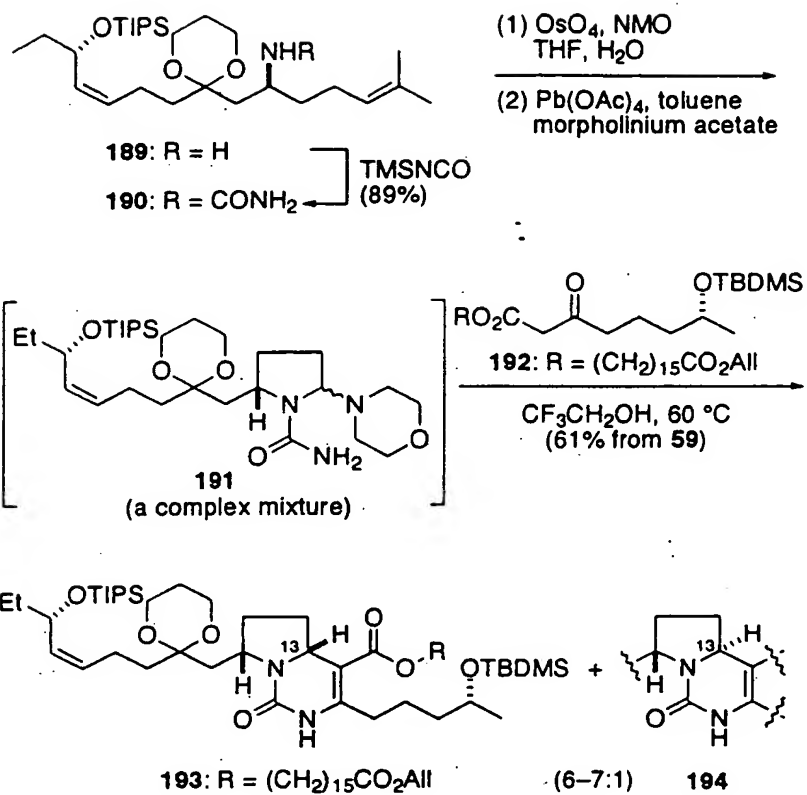
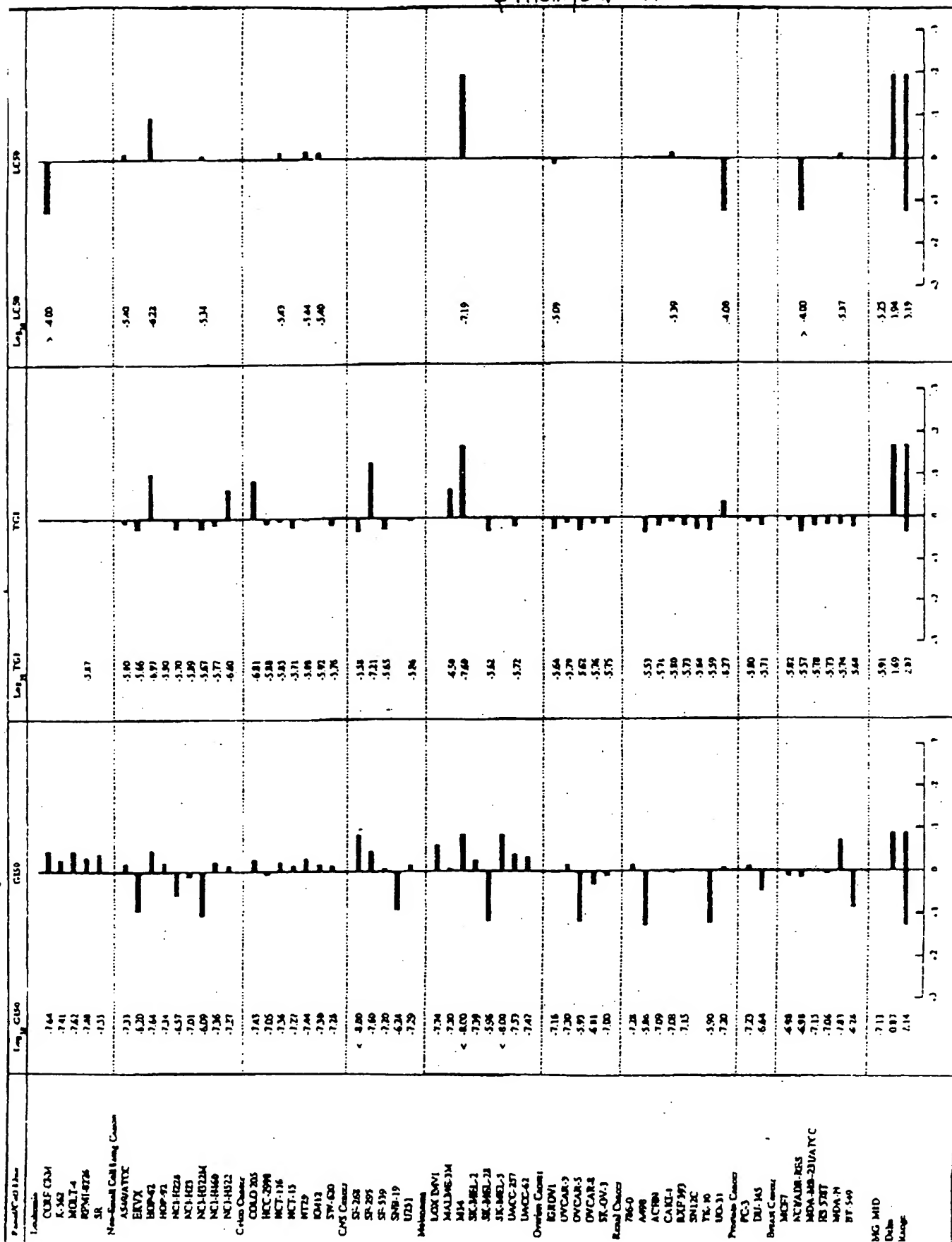


Figure 55

Mean Graphs



National Cancer Institute Developmental Therapeutics Program

Mean Graphs

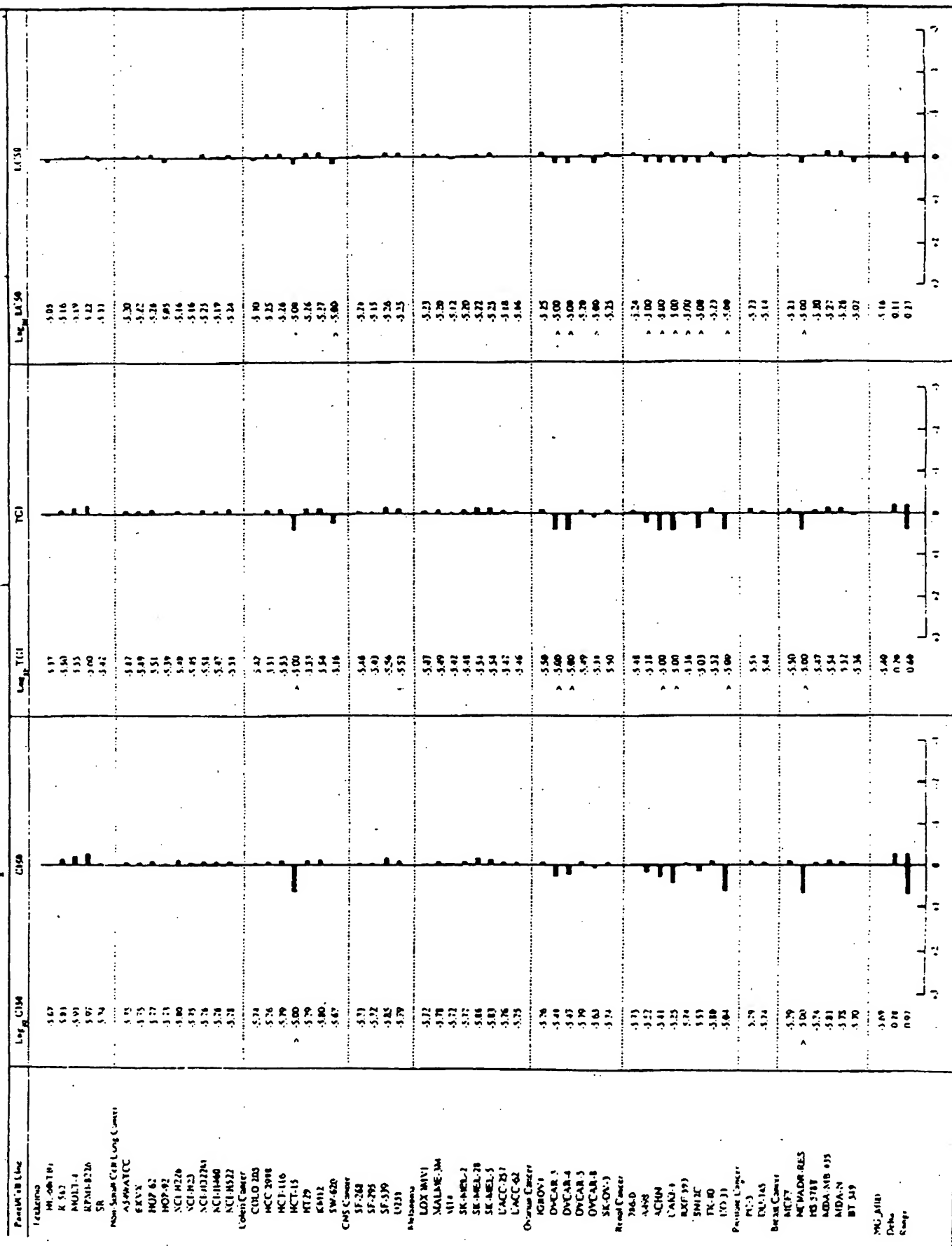
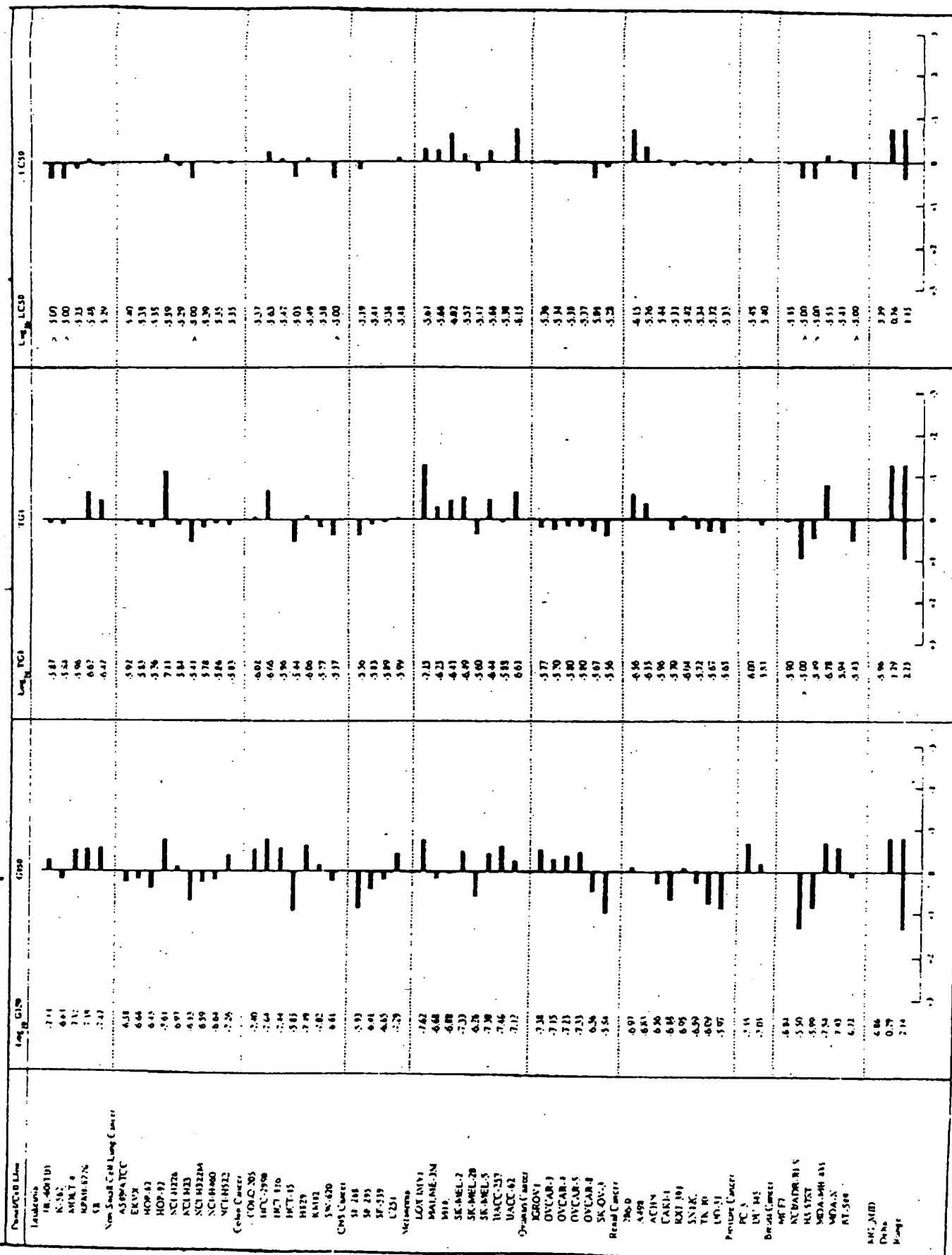


Figure 57

Mean Graphs



Mean Graphs

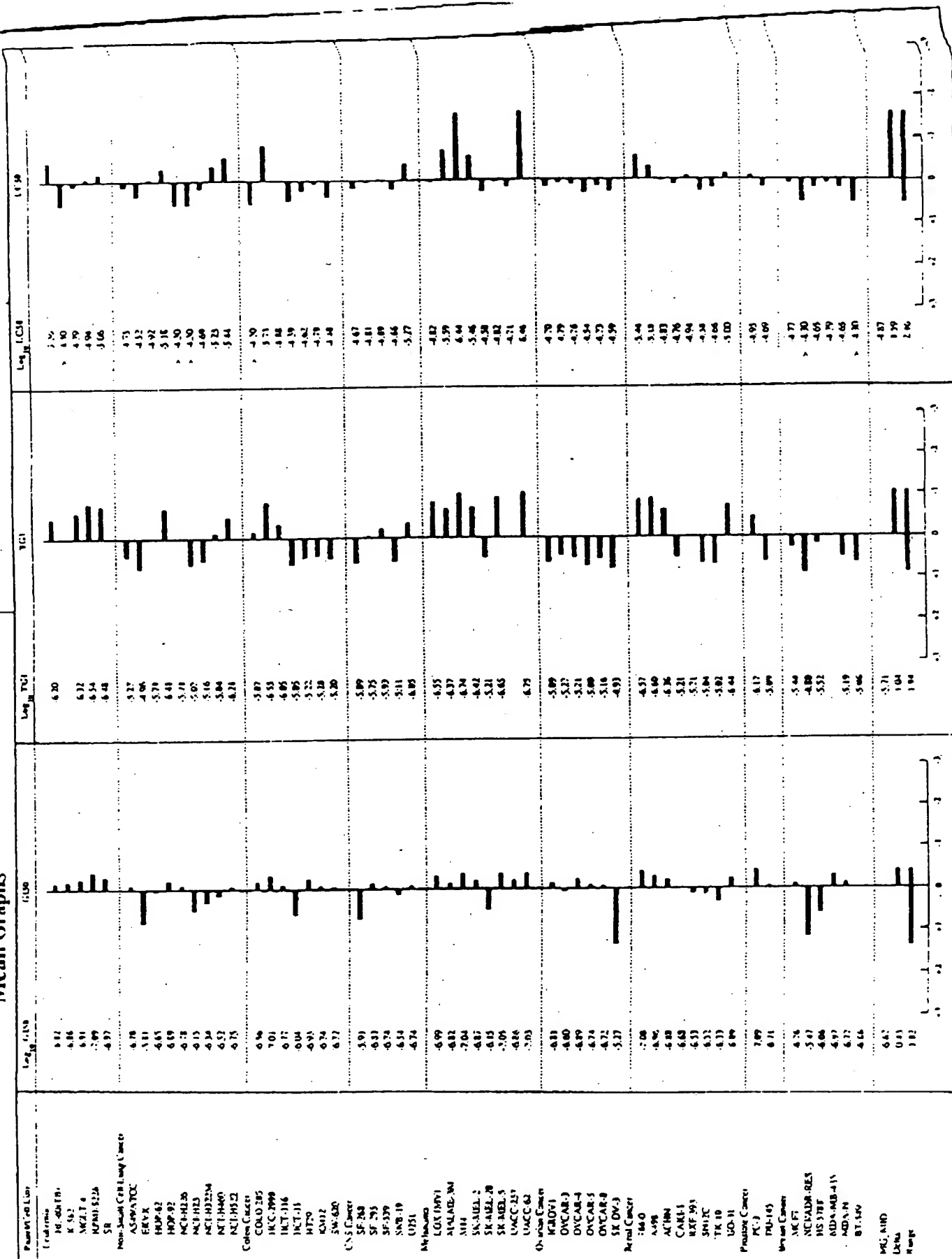


Figure 59

Mean Graphs

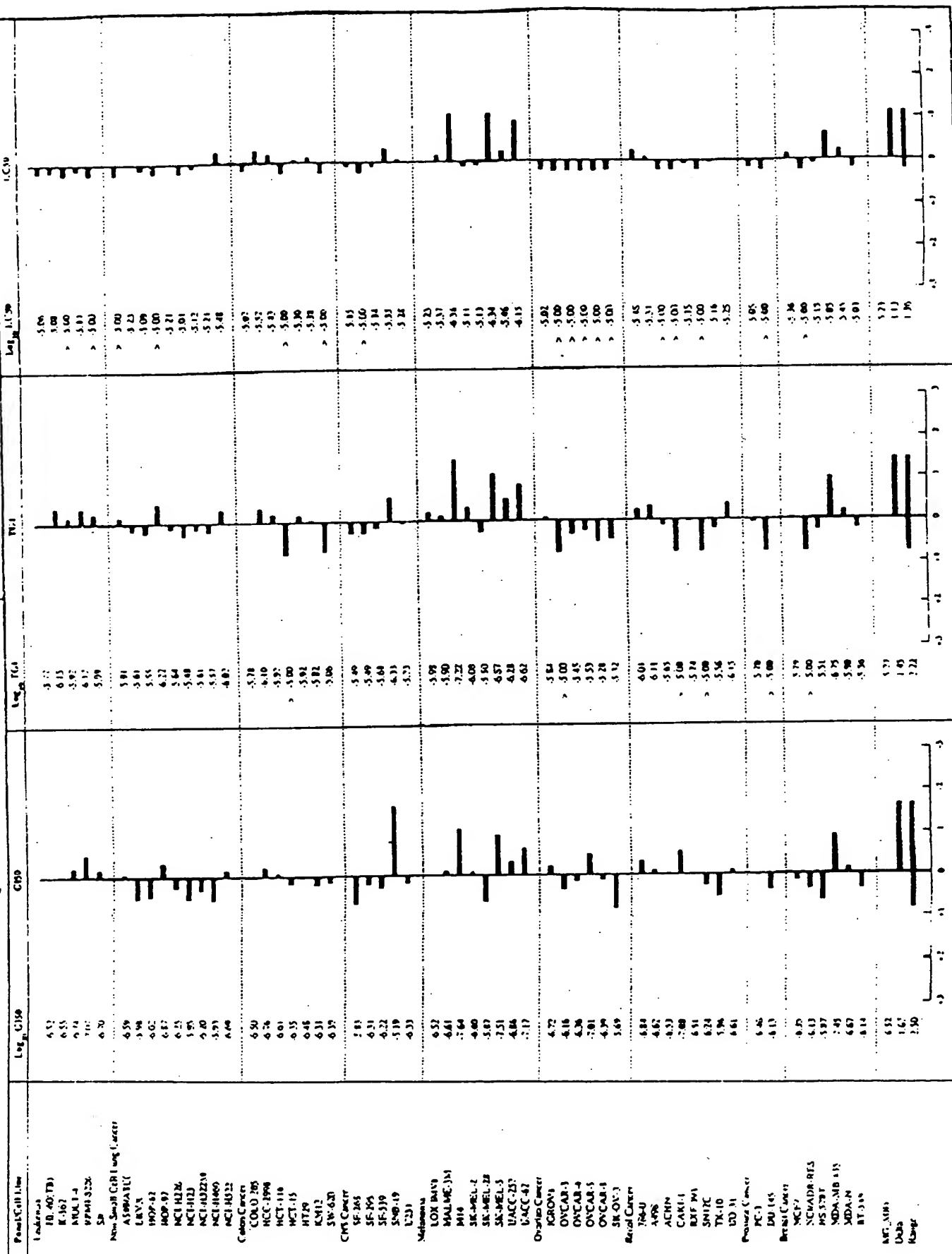
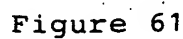


Figure 60

Mean (Graphs)



Mean Graphs

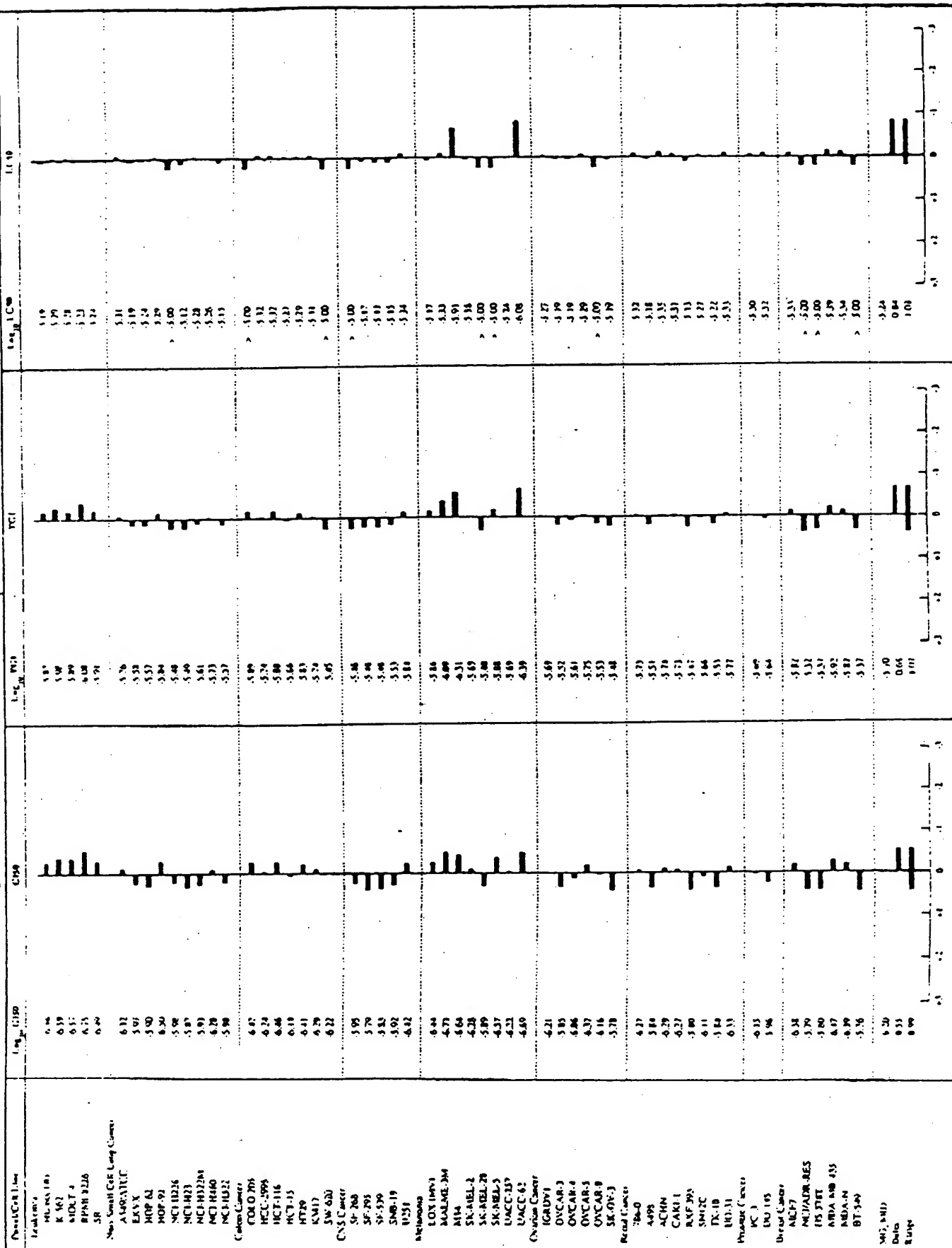


Figure 62